Search report

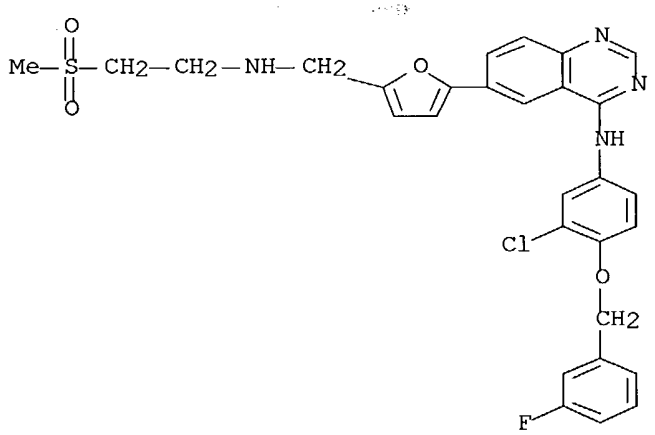
L4 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:533970 CAPLUS Full-text
DN 141:65088
TI Methods and compositions for the prevention or treatment of neoplasia comprising a COX-2 inhibitor in combination with an epidermal growth factor receptor antagonist
IN Masferrer, Jaime
PA Pharmacia Corporation, USA
SO U.S. Pat. Appl. Publ., 103 pp., Cont.-in-part of U.S. Ser. No. 470,951.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 21

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004127470	A1	20040701	US 2003-651916	20030829
PRAI	US 1998-113786P	P	19981223		
	US 1999-470951	B2	19991222		

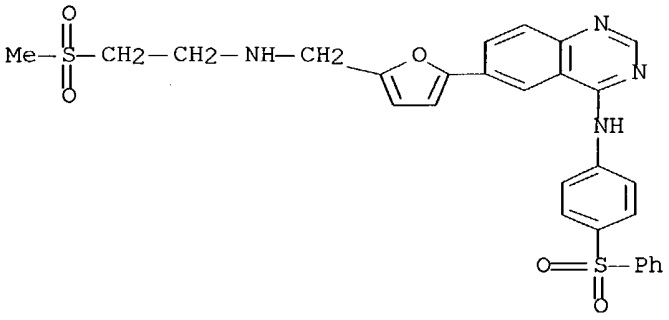
AB The present invention relates to a novel method of preventing and/or treating neoplasia disorders in a subject that is in need of such prevention or treatment by administering to the subject at least one COX-2 inhibitor in combination with an EGF receptor antagonist. Compns., pharmaceutical compns. and kits are also described.

IT **231277-92-2**, GW572016 **386744-56-5**, GW 9525
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as EGFR antagonist; COX-2 inhibitor in combination with epidermal growth factor receptor antagonist for prevention or treatment of neoplasia)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 386744-56-5 CAPLUS
CN 4-Quinazolinamine, 6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-N-[4-(phenylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)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L4 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:336121 CAPLUS Full-text
DN 140:399538
TI Inhibition of ErbB1 and ErbB2 by lapatinib ditosylate, a dual kinase inhibitor: Promising activity in pretreated advanced breast cancer
AU Maung, Kavita; O'Shaughnessy, Joyce A.
CS USA
SO Clinical Breast Cancer (2004), 4(6), 398-400
CODEN: CBCLB7; ISSN: 1526-8209
PB Cancer Information Group, LP
DT Journal
LA English
AB This article discusses the efficacy of lapatinib ditosylate, an inhibitor of the ErbB1 and ErbB2 kinase in patients with advanced breast cancer.
IT **388082-77-7**, Lapatinib ditosylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy of lapatinib ditosylate in pretreated advanced breast cancer)
RN 388082-77-7 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-, bis(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

CRN 231277-92-2
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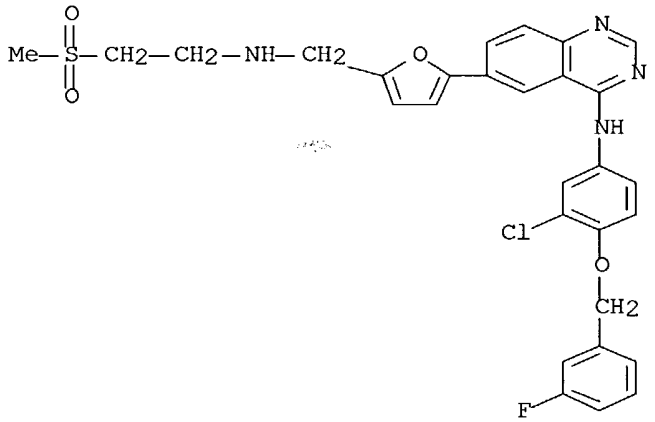

CM 2

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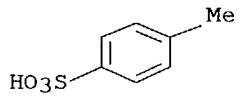
CMF C7 H8 O3 S



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:100947 CAPLUS Full-text
DN 140:139486
TI Method of treating cancer
IN Potter, David A.
PA Advanced Research & Technology Institute at Indiana University, USA
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004010937	A2	20040205	WO 2003-US23437	20030728
	WO 2004010937	A3	20040527		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU

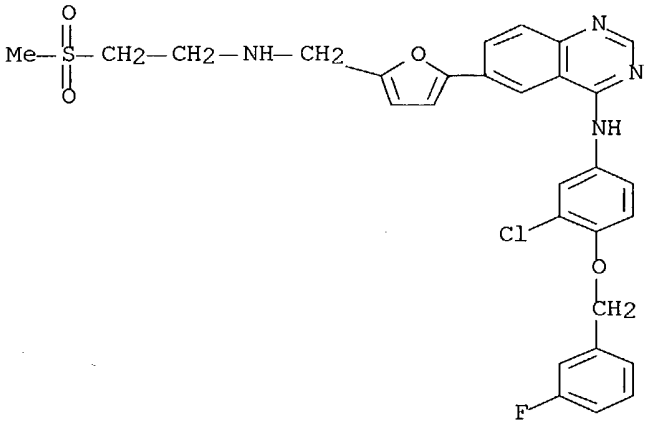
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-399573P P 20020726

AB Methods for treating cancer are described here. The methods include administering to an HIV-neg. patient an m-calpain inhibitor such as ritonavir. Ritonavir or other m-calpain inhibitors can also be co-administered with other therapeutic agents such as a Cox-2 inhibitor, a taxane, or a proteasome inhibitor. Methods for determining whether a patient will respond to a particular method of treatment are also described herein.

IT **231277-92-2**, GW 572016
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating cancer)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)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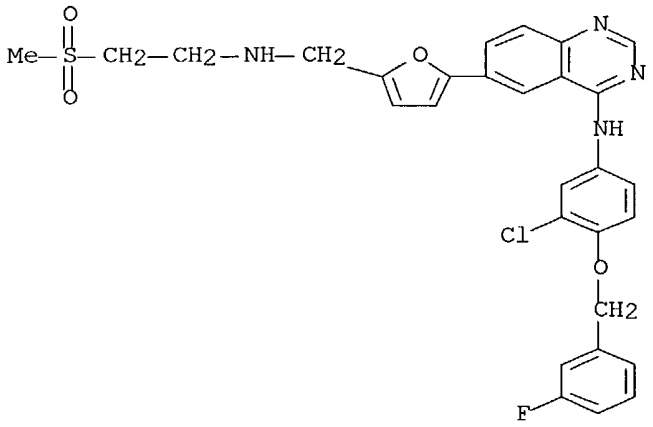
L4 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:52260 CAPLUS Full-text
DN 140:297018
TI Truncated ErbB2 receptor (p95ErbB2) is regulated by heregulin through heterodimer formation with ErbB3 yet remains sensitive to the dual EGFR/ErbB2 kinase inhibitor GW572016
AU Xia, Wenle; Liu, Lei-Hua; Ho, Peter; Spector, Neil L.
CS Department of Discovery Medicine, GlaxoSmithKline, Research Triangle Park,
NC, 27709-3398, USA
SO Oncogene (2004), 23(3), 646-653
CODEN: ONCNES; ISSN: 0950-9232
PB Nature Publishing Group
DT Journal
LA English
AB The expression of the NH2 terminally truncated ErbB2 receptor (p95ErbB2) in breast cancer correlates with metastatic disease progression compared with the expression of full-length p185ErbB2. We now show that heregulin (HRG), but not EGF, stimulates p95ErbB2 phosphorylation in BT474 breast cancer cells. Furthermore, phospho-p95ErbB2 forms heterodimers with ErbB3, but not EGFR, while p185ErbB2 heterodimerizes with both EGFR and ErbB3. The predilection of p95ErbB2 to heterodimerize with ErbB3 provides an explanation for its regulation by HRG, an ErbB3 ligand. GW572016, a reversible small mol. inhibitor of EGFR and ErbB2 tyrosine kinases, inhibits baseline p95ErbB2 phosphorylation in BT474 cells and tumor xenografts. Inhibition of p95ErbB2, p185ErbB2, and EGFR phosphorylation by GW572016 resulted in the inhibition of downstream phospho-Erk1/2, phospho-AKT, and cyclin D steady-state protein levels. Increased phosphorylation of p95ErbB2 and AKT in response to HRG was abrogated to varying degrees by GW572016. In contrast, trastuzumab did not inhibit p95ErbB2 phosphorylation or the expression of downstream phospho-Erk1/2, phospho-AKT, or cyclin D. It is tempting to speculate that trastuzumab resistance may be mediated in part by the selection of p95ErbB2-expressing breast cancer cells capable of exerting potent growth and prosurvival signals through p95ErbB2-ErbB3 heterodimers. Thus, p95ErbB2 represents a target for therapeutic intervention, and one that is sensitive to GW572016 therapy.
IT **231277-92-2**, GW572016
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(truncated ErbB2 receptor (p95ErbB2) is regulated by heregulin through
heterodimer formation with ErbB3 yet remains sensitive to the dual EGFR/ErbB2 kinase inhibitor GW572016)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:41317 CAPLUS Full-text
DN 140:99649
TI Pharmaceutical compositions for the treatment of respiratory tract diseases comprising novel anticholinergic agents and inhibitors of EGFR-kinase
IN Pairet, Michel; Meade, Christopher John Montague; Pieper, Michael P.
PA Boehringer Ingelheim Pharma Gmbh & Co. Kg, Germany
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004004775	A1	20040115	WO 2003-EP6788	20030626
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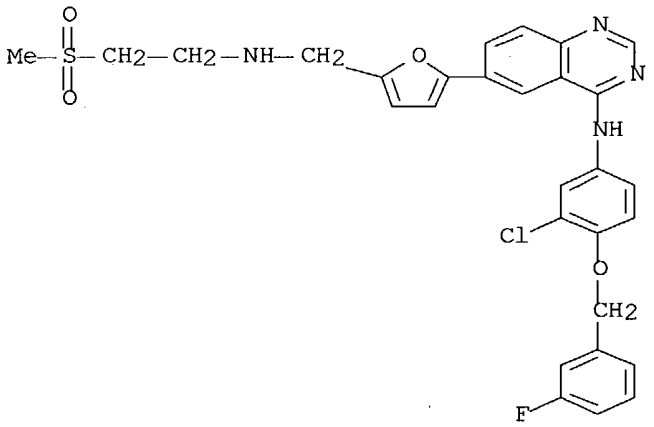
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10230751	A1	20040122	DE 2002-10230751	20020709
	US 2004048887	A1	20040311	US 2003-614382	20030707
PRAI	DE 2002-10230751	A	20020709		
	US 2002-407746P	P	20020903		

OS MARPAT 140:99649
AB The invention relates to novel pharmaceutical compns. comprising novel anticholinergic agents and EGFR-kinase inhibitors, method for production and use thereof in the treatment of respiratory diseases. The synthesis of several EGFR-kinase inhibitors is given. Thus an inhalation capsule contained (microgram/capsule): 2,2-Diphenylpropionic acid scopine ester methobromide 60; EGFR kinase inhibitor 3500; lactose 3440.
IT **231277-92-2**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. for treatment of respiratory tract diseases comprising anticholinergic agents and inhibitors of EGFR-kinase)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:2613 CAPLUS Full-text
DN 140:53400
TI Cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy
IN Bacus, Sarah S.
PA Ventana Medical Systems, Inc., USA
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004000101	A2	20031231	WO 2003-US19697	20030619

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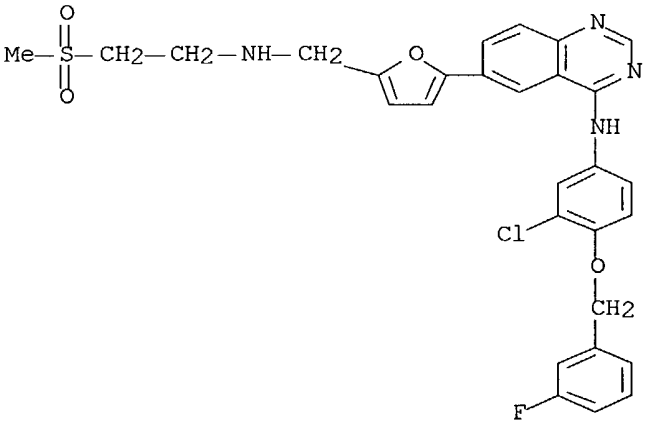
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-389795P P 20020619
US 2002-432811P P 20021211

AB This invention provides methods for determining or predicting response to HER1/HER2-directed cancer therapy in an individual. The methodol. of the invention includes assaying a tumor sample with one or more reagents that detect expression and/or activation of predictive biomarkers for cancer, e.g. growth factor receptors, growth factor receptor ligands, and growth factor receptor-related downstream signaling mols.

IT **231277-92-2**, GW572016
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cancer biomarker expression/activation-based method for predicting response to HER1/HER2-directed cancer therapy)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)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L4 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:2612 CAPLUS Full-text
DN 140:53399
TI Predictive markers in cancer therapy
IN Bacus, Sarah S.; Herrle, Myra R.; Kirk, L. Edward; Spector, Neil L.; Stocum, Michael T.; Xia, Wenle
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004000094	A2	20031231	WO 2003-US12739	20030424

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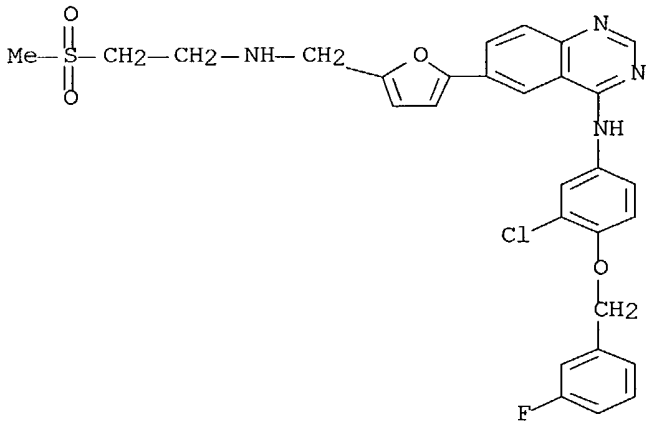
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-389795P P 20020619
US 2002-432811P P 20021211
US 2002-432943P P 20021211
US 2003-451978P P 20030303

AB Mol. markers useful in medicine response tests are provided, as an aid in determining whether an individual subject's tumor is responding to treatment with EGF and/or erbB2 inhibitors. Markers include phosphorylated ERK protein.

IT **231277-92-2**, GW572016
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(predictive markers in cancer therapy)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)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L4 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:971922 CAPLUS Full-text
DN 140:23220
TI Preventives and/or remedies for subjects with the expression or activation
of her2 and/or EGFR
IN Suzuki, Tsuyoshi; Kitano, Yasunori; Yano, Shinji
PA Mitsubishi Pharma Corporation, Japan
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003101491	A1	20031211	WO 2003-JP6988	20030603

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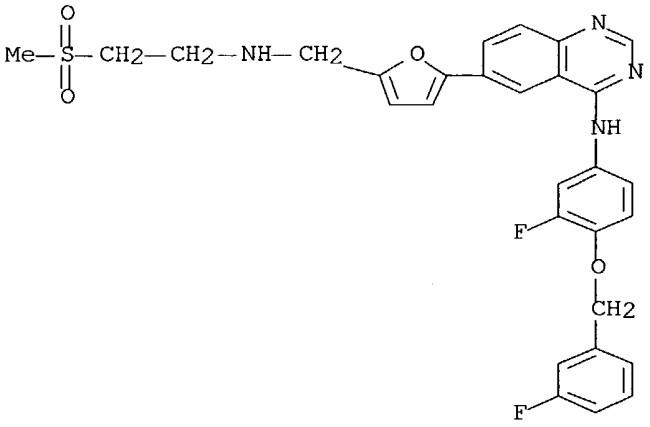
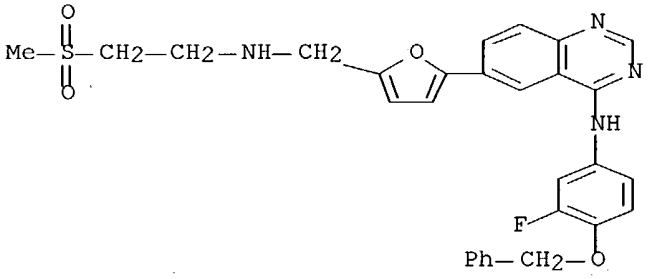
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI JP 2002-162130 A 20020603
OS MARPAT 140:23220
AB Her2 and/or EGFR inhibitors to be administered to subjects with the overexpression or activation of Her2 and/or EGFR that have been subjected to an examination for detecting the expression or activity of Her2 and/or EGFR and thus regarded as having the overexpression or activation of Her and/or EGFR; and medicinal compns. containing such an inhibitor.
IT **231277-81-9 231277-90-0 231277-91-1**
231277-92-2 231278-00-5 231278-05-0
386744-56-5 633370-23-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinazoline analogs as preventives and/or remedies for subjects with the expression or activation of her2 and/or EGFR)
RN 231277-81-9 CAPLUS
CN 4-Quinazolinamine, N-[3-fluoro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 231277-90-0 CAPLUS
CN 4-Quinazolinamine, N-[3-fluoro-4-(phenylmethoxy)phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 231277-91-1 CAPLUS
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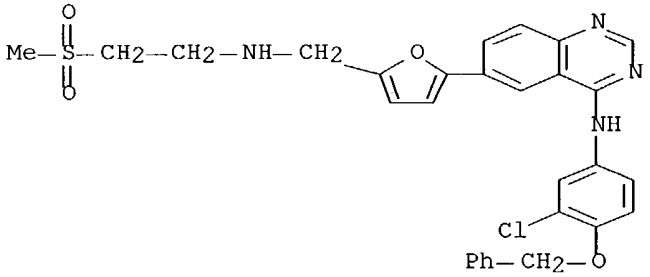
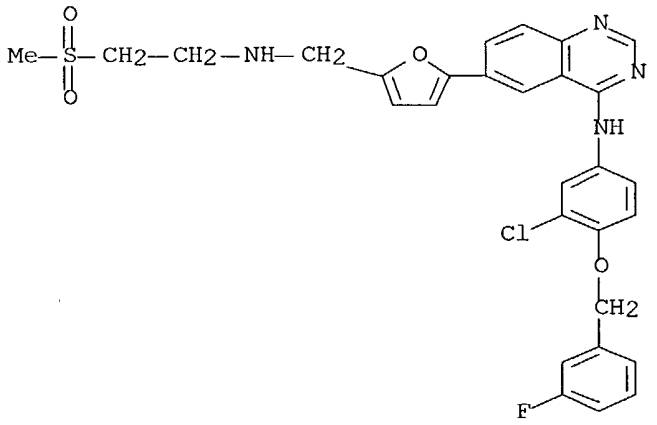
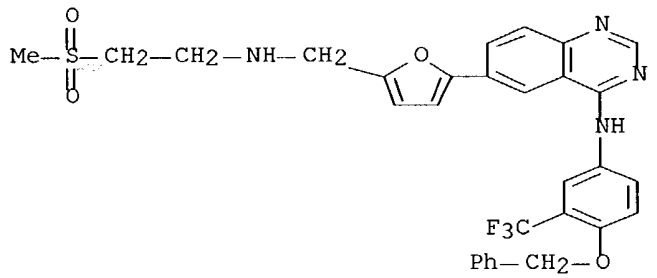


RN 231277-92-2 CAPLUS

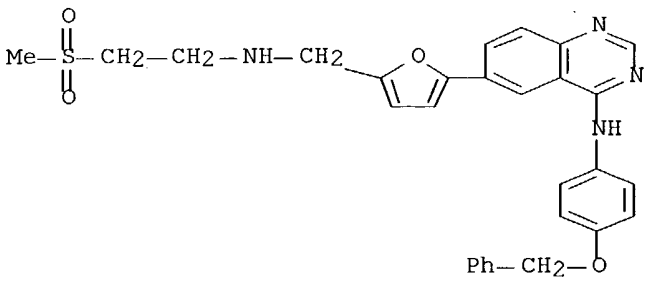
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



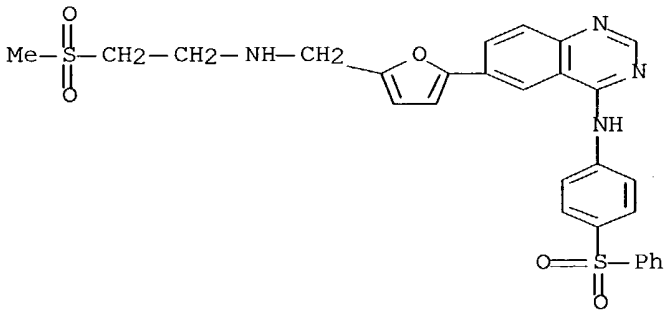
RN 231278-00-5 CAPLUS
CN 4-Quinazolinamine, 6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-N-[4-(phenylmethoxy)-3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



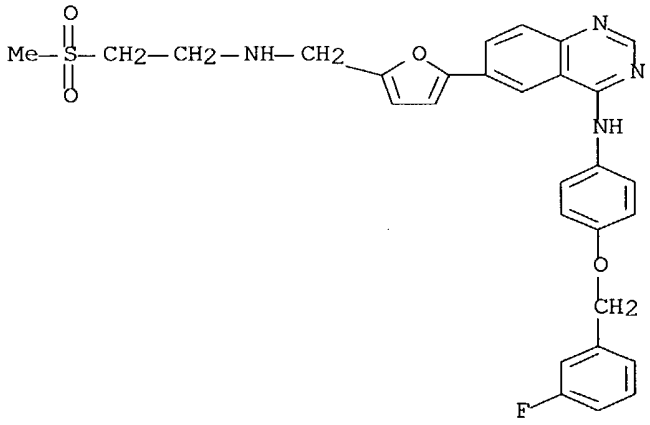
RN 231278-05-0 CAPLUS
CN 4-Quinazolinamine, 6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-N-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



RN 386744-56-5 CAPLUS
CN 4-Quinazolinamine, 6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-N-[4-(phenylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

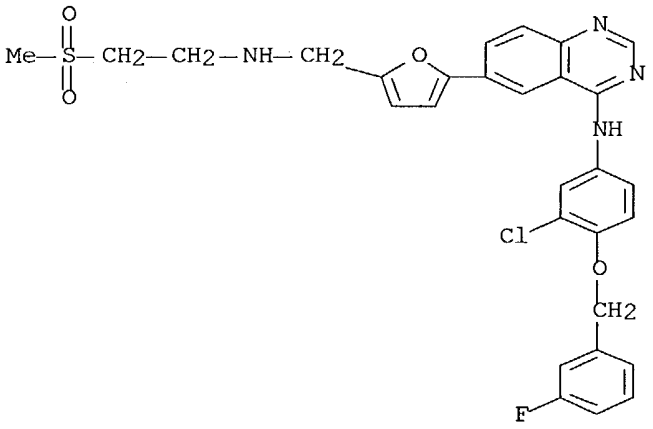


RN 633370-23-7 CAPLUS
CN 4-Quinazolinamine, N-[4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:917646 CAPLUS Full-text
DN 140:38051
TI Epidermal Growth Factor Receptor Autocrine Signaling in RIE-1 Cells Transformed by the Ras Oncogene Enhances Radiation Resistance
AU Grana, Theresa M.; Sartor, Carolyn I.; Cox, Adrienne D.
CS Curriculum in Genetics and Molecular Biology, Department of Radiation Oncology, University of North Carolina, Chapel Hill, NC, USA
SO Cancer Research (2003), 63(22), 7807-7814
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Oncogenic forms of the small GTPase Ras increase the resistance of cells to killing by ionizing radiation (IR). Although not all of the signaling pathways for radioresistance are well defined, it is now clear that Ras-dependent signaling pathways involved in radioresistance include those mediated by phosphatidylinositol 3'-kinase (PI3-K) and Raf. Nevertheless, PI3-K and Raf together are not sufficient to reconstitute all of the resistance conferred by Ras, indicating that other effectors must also contribute. We show here that Ras-driven autocrine signaling through the epidermal growth factor receptor (EGFR) also contributes to radioresistance in Ras-transformed cells. Conditioned media (CM) collected from RIE-1 rat intestinal epithelial cells expressing oncogenic Ras increased the survival of irradiated cells. Ras-CM contains elevated levels of the EGFR ligand transforming growth factor α (TGF-α). Both Ras-CM and TGF-α stimulated EGFR phosphorylation, and exogenous TGF-α mimicked the effects of Ras-CM to increase radioresistance. Blocking EGFR signaling with the EGFR/HER-2 kinase inhibitor (KI) GW572016 decreased the postradiation survival of irradiated Ras-transformed cells and normal cells but had no effect on the survival of unirradiated cells. Ras-CM and TGF-α also increase PI3-K activity downstream of the EGFR and increase postradiation survival, both of which are abrogated by GW572016. Thus, Ras utilizes autocrine signaling through EGFR to increase radioresistance, and the EGFR KI GW572016 acts as a radiosensitizer. The observation that Ras-transformed cells can be sensitized to killing by ionizing radiation with GW572016 demonstrates that EGFR KIs could potentially be used to radiosensitize tumors in which radioresistance is dependent on Ras-driven autocrine signaling through EGFR.
IT **231277-92-2**, GW572016
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Ras utilizes autocrine signaling through EGF receptor to increase radioresistance in Ras-transformed cells and GW572016 acts as a radiosensitizer)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

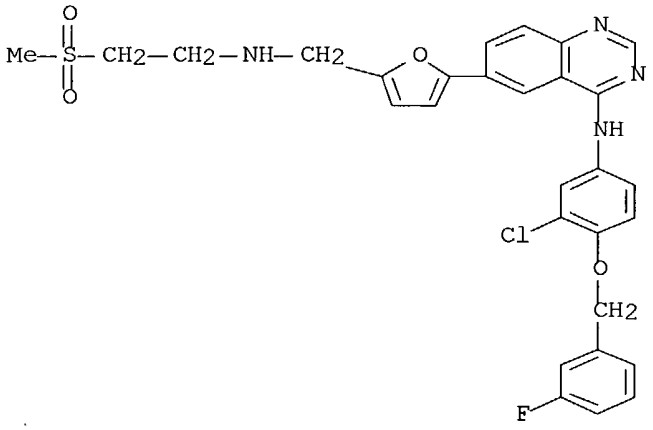


RE.CNT 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:913005 CAPLUS Full-text
DN 139:391384
TI Use of inhibitors of EGFR-mediated signal transduction for the treatment of benign prostatic hyperplasia (BPH)/prostatic hypertrophy
IN Singer, Thomas; Colbatzky, Florian; Platz, Stefan
PA Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003094921	A2	20031120	WO 2003-EP4606	20030502
	WO 2003094921	A3	20040318		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10221018	A1	20031127	DE 2002-10221018	20020511
	US 2003225079	A1	20031204	US 2003-431699	20030508
PRAI	DE 2002-10221018	A	20020511		
	US 2002-389815P	P	20020618		

OS MARPAT 139:391384
AB The invention discloses the use of EGF-receptor antagonists for the production of a medicament to prevent and/or treat benign prostatic hyperplasia and/or prostatic hypertrophy, as well as a method for the treatment or prevention of benign prostatic hyperplasia/prostatic hypertrophy involving the administration of an EGF-receptor antagonist, optionally in combination with known compds. for the treatment of benign prostatic hyperplasia/prostatic hypertrophy, and the corresponding pharmaceutical compns. Compds. of the invention include e.g. quinazoline derivs. and monoclonal antibodies. Preparation of 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4- (N-(2-methoxyethyl)-N-methylamino)-1-oxo-2-buten-1-yl)amino]-7- cyclopropylmethoxyquinazoline is described.
IT **231277-92-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(EGFR-mediated signal transduction inhibitors for treatment of benign prostatic hyperplasia/prostatic hypertrophy)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

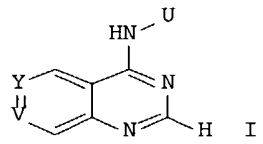

O
Me—S— CH2— CH2— NH— CH2
O
O
N
N
NH
Cl
O
CH2
F

L4 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:836903 CAPLUS Full-text
DN 139:317433
TI Cancer treatment method comprising administering an erb-family inhibitor and a raf and/or ras inhibitor
IN Spector, Neil Lee; Xia, Wenle
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086467	A1	20031023	WO 2003-US10747	20030408

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

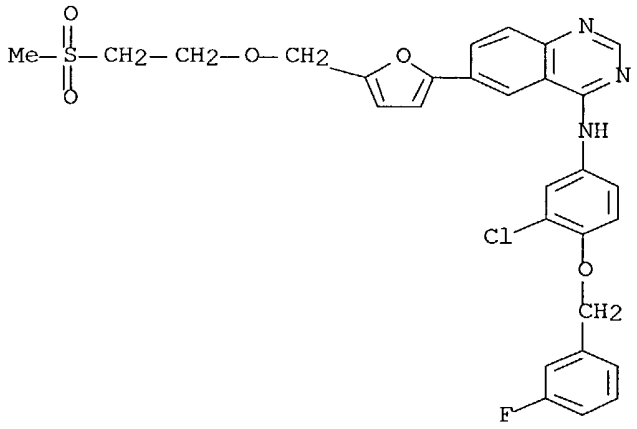
PRAI US 2002-370807P P 20020408
OS MARPAT 139:317433
GI



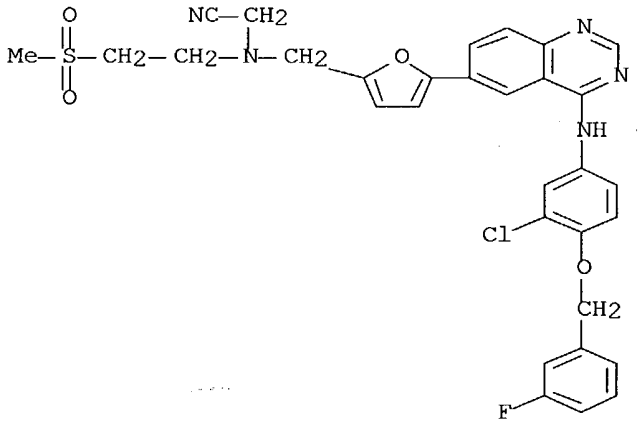
I

AB The invention provides a method for treating cancer in a mammal, as well as pharmaceutical combinations useful in such treatment. In particular, the method relates to a cancer treatment method that includes administering an erb family inhibitor and a Raf and/or ras inhibitor to a mammal suffering from a cancer. Preparation of compds., e.g. erbB-2/EGFR inhibitor I, is described.

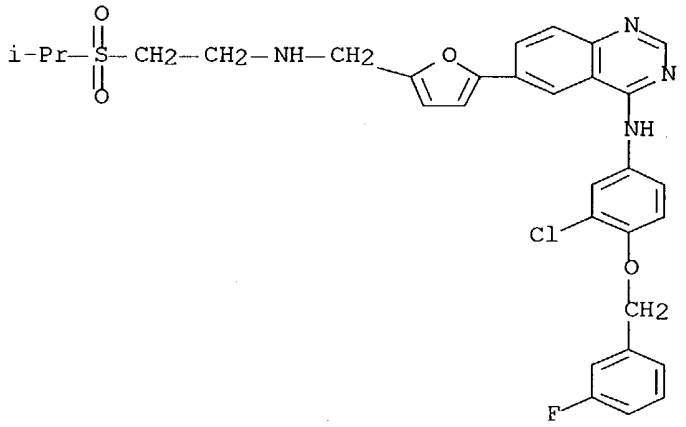
IT **319917-44-7P 319917-46-9P 320337-12-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)
RN 319917-44-7 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[2-(methylsulfonyl)ethoxy]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 319917-46-9 CAPLUS
CN Acetonitrile, [[[5-[4-[[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]amino]-6-quinazolinyl]-2-furanyl]methyl][2-(methylsulfonyl)ethyl]amino]- (9CI)(CA INDEX NAME)



RN 320337-12-0 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-[(1-methylethyl)sulfonyl]ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

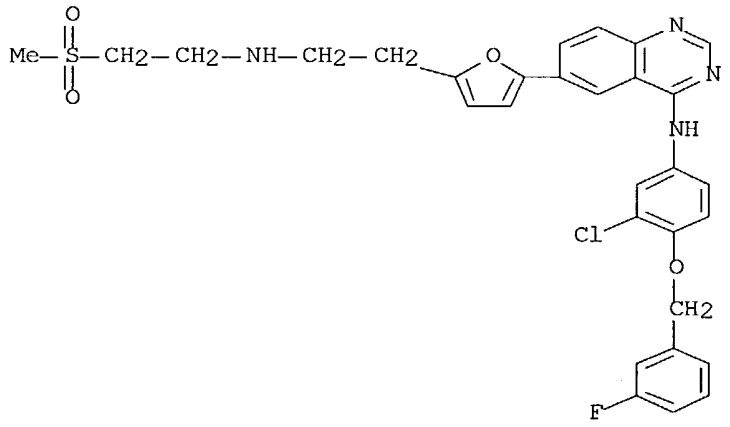


IT **319917-43-6**

RL: RCT (Reactant); RACT (Reactant or reagent)
(erb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)

RN 319917-43-6 CAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[2-[[2-(methylsulfonyl)ethyl]amino]ethyl]-2-furanyl]- (9CI) (CA INDEX NAME)

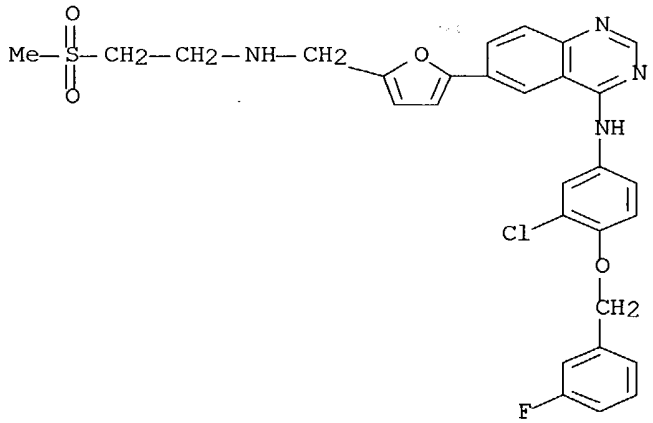


IT **231277-92-2P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(nod nherb-family inhibitor and raf and/or ras inhibitor combination for cancer treatment)

RN 231277-92-2 CAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

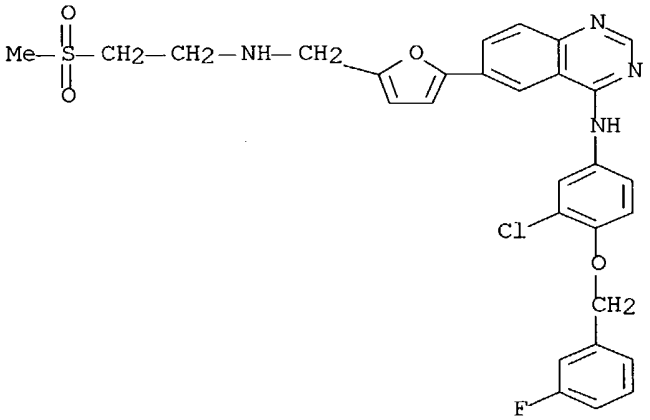


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:818866 CAPLUS Full-text
DN 140:104
TI Lapatinib ditosylate (GlaxoSmithKline
AU Kim, Tracy E.; Murren, John R.
CS Beverly Hills, CA, 90211, USA
SO IDrugs (2003), 6(9), 886-893
CODEN: IDRUFN; ISSN: 1369-7056
PB Current Drugs
DT Journal; General Review
LA English
AB A review. Lapatinib ditosylate, an ErbB-2 and EGFR dual tyrosine kinase inhibitor, is being developed by GlaxoSmithKline plc for the potential treatment of solid tumors.
IT **388082-77-7**, Lapatinib ditosylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)(lapatinib ditosylate for potential treatment of solid tumors)
RN 388082-77-7 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-, bis(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

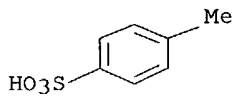
CM 1

CRN 231277-92-2
CMF C29 H26 Cl F N4 O4 S



CM 2

CRN 104-15-4
CMF C7 H8 O3 S



RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:719350 CAPLUS Full-text
DN 139:239200
TI Apparatus and method for separating and collecting particles
IN Franklin, Michael Leon
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003074154	A1	20030912	WO 2003-US5645	20030226

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-360734P P 20020301

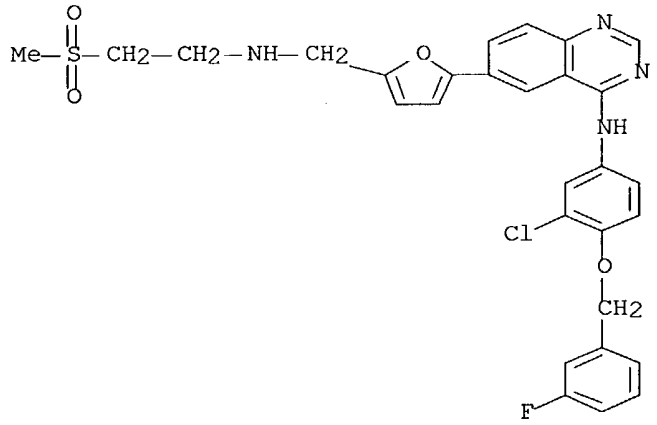
AB An apparatus for use in the separation and collection of particles comprises a base member including a particle collection surface, a lateral wall such as a cylinder disposed on the base member, and a cover member disposed on the lateral wall. The cover member, the lateral wall and the base member cooperatively define an enclosed particle settling-chamber. A particle sample holder is mounted within the particle settling-chamber at a distance above the particle collection surface. In use, a propellant ejection device having a propellant ejection outlet operatively directed toward the particle sample holder is used to deliver a metered quantity of propellant toward the particle sample holder to disperse particles within the chamber. The dispersed particles settle onto the particle collection surface, and the particle collection surface can then be removed from the apparatus for subsequent use in particle anal. procedures.

IT **388082-78-8**
RL: NUU (Other use, unclassified); USES (Uses)
(apparatus and method for separating and collecting particles)

RN 388082-78-8 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-, bis(4-methylbenzenesulfonate), monohydrate (9CI) (CA INDEX NAME)

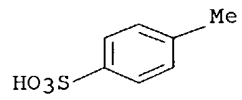
CM 1

CRN 231277-92-2
CMF C29 H26 Cl F N4 O4 S



CM 2

CRN 104-15-4
CMF C7 H8 O3 S



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:607455 CAPLUS Full-text
DN 139:159940
TI Use of tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions
IN Jung, Birgit; Puschner, Hubert
PA Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SO Ger. Offen., 24 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10204462	A1	20030807	DE 2002-10204462	20020205
	WO 2003066060	A2	20030814	WO 2003-EP814	20030128
	WO 2003066060	A3	20040115		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

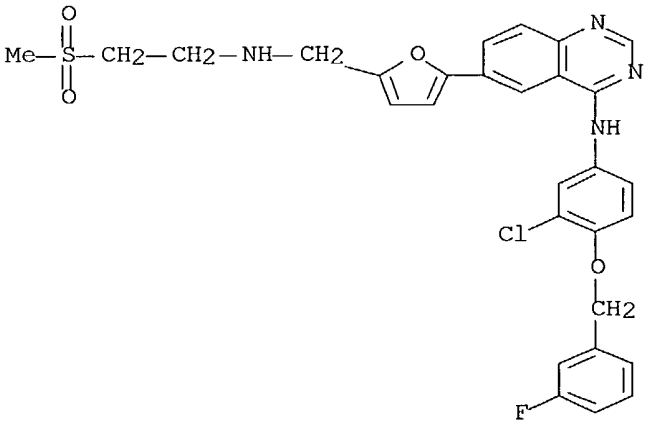
	US 2003149062	A1	20030807	US 2003-353616	20030129
PRAI	DE 2002-10204462	A	20020205		

OS MARPAT 139:159940

AB The invention discloses the use of quinazoline derivs. (Markush included), or the compds. (1) 4-[(3-chloro-4-fluorphenyl)amino]-6-[(4-dimethylaminocyclohexyl)amino]pyrimido[5,4-d]pyrimidine; (2) 4-[(R)-(1-phenylethyl)amino]-6-(4-hydroxyphenyl)-7H-pyrrolo[2,3- d]pyrimidine; (3) 4-[(3-Chloro-4-(3-fluoro-4-benzyloxy)phenyl)amino]-6-[5- (((2-methansulfonylethyl)amino)methyl)-furan-2-yl]quinazoline; or the antibody cetuximab C225, trastuzumab, ABX-EGF, Mab ICR-62 and EGFR antisense, their tautomers, their stereoisomers and their salts, in particular their physiol. compatible salts with inorg. or organic acids or bases, for the production of a medication for prevention or treatment of diseases of the respiratory system or the lung. Preparation of quinazoline compds. is included.

IT **231277-92-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions)

RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)


O
Me—S—CH2—CH2—NH—CH2
O
O
N
N
NH
Cl
O
CH2
F

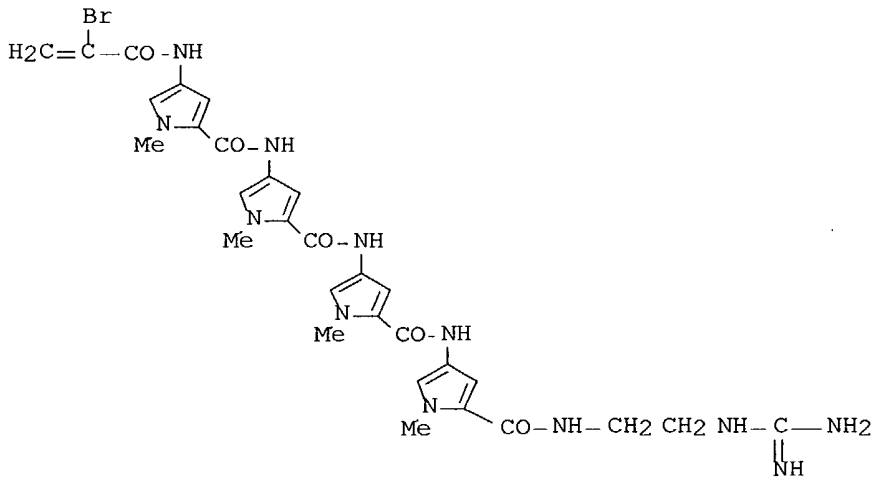
L4 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:532545 CAPLUS Full-text
DN 139:95455
TI Combined therapy against tumors comprising substituted acryloyl distamycin
derivatives and protein kinase (serine/threonine kinase) inhibitors
IN Geroni, Maria Cristina; Fowst, Camilla; Cozzi, Paolo
PA Pharmacia Italia SpA, Italy
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003055522	A1	20030710	WO 2002-EP13092	20021218

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2002-75052 A 20020102
OS MARPAT 139:95455
GI

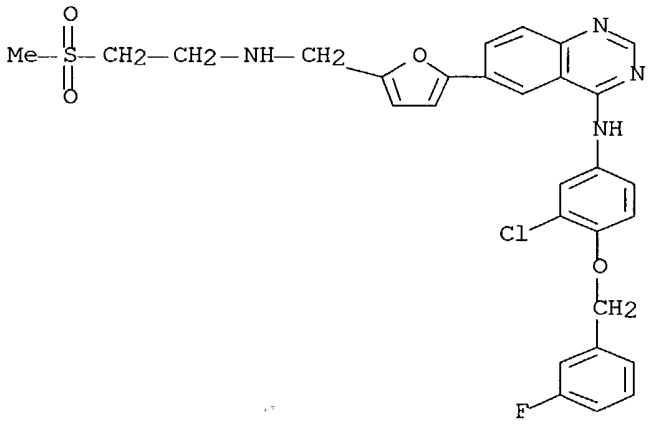


AB The present invention provides the combined use of acryloyl distamycin derivs., in particular α-bromo- and α-chloro-acryloyl distamycin derivs., and a protein kinase (serine/threonine and tyrosine kinases) inhibitor, in the treatment of tumors. Also provided is the use of the said combinations in the treatment or prevention of metastasis or in the treatment of tumors by inhibition of angiogenesis. An example protein kinase inhibitor is STI 571 and a distamycin derivative is brostallicin (I).

IT **231277-92-2**, GW572016
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined antitumor therapy comprising acryloyl distamycin derivs. and
protein kinase (serine/threonine kinase) inhibitors)

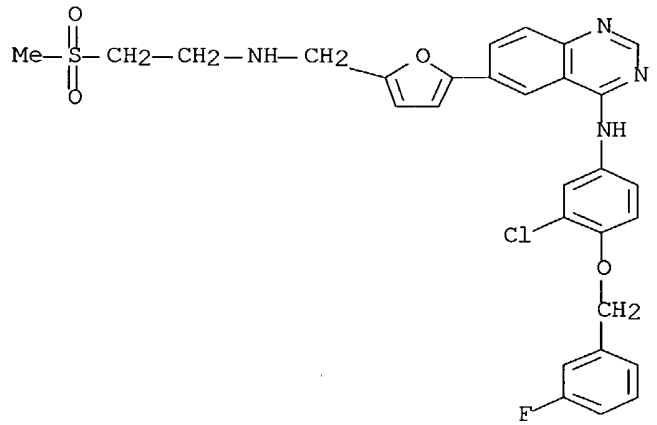
RN 231277-92-2 CAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



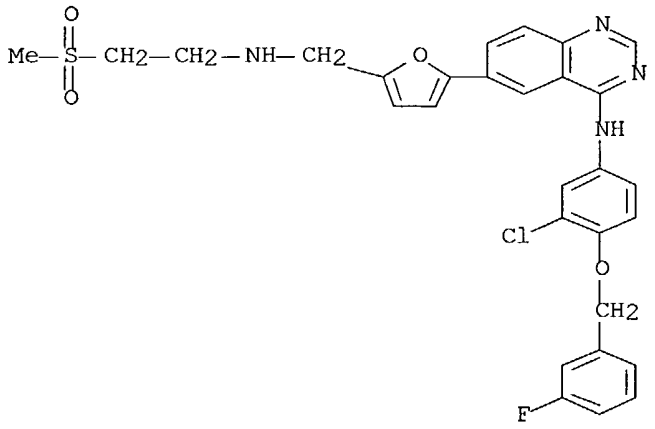
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:8967 CAPLUS Full-text
DN 139:62338
TI Small molecule tyrosine kinase inhibitors: clinical development of anticancer agents
AU Laird, A. Douglas; Cherrington, Julie M.
CS SUGEN, Inc., South San Francisco, CA, 94080, USA
SO Expert Opinion on Investigational Drugs (2003), 12(1), 51-64
CODEN: EOIDER; ISSN: 1354-3784
PB Ashley Publications Ltd.
DT Journal; General Review
LA English
AB A review. Numerous small mol. synthetic tyrosine kinase inhibitors are in clin. development for the treatment of human cancers. These fall into three broad categories: inhibitors of the epidermal growth factor receptor tyrosine kinase family (e.g., Iressa and Tarceva), inhibitors of the split kinase domain receptor tyrosine kinase subgroup (e.g., PTK787/ZK 222584 and SU11248) and inhibitors of tyrosine kinases from multiple subgroups (e.g., Gleevec). In addition, agents targeting other tyrosine kinases implicated in cancer, such as Met, Tie-2 and Src, are in preclin. development. As experience is gained in the clinic, it has become clear that unleashing the full therapeutic potential of tyrosine kinase inhibitors will require patient preselection, better assays to guide dose selection, knowledge of mechanism-based side effects and ways to predict and overcome drug resistance.
IT **231277-92-2**, GW-572016
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small mol. tyrosine kinase inhibitors and clin. development of anticancer agents)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RE.CNT 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:668812 CAPLUS Full-text
DN 138:280796
TI Anti-tumor activity of GW572016: a dual tyrosine kinase inhibitor blocks EGF activation of EGFR/erbB2 and downstream Erk1/2 and AKT pathways
AU Xia, Wenle; Mullin, Robert J.; Keith, Barry R.; Liu, Lei-Hua; Ma, Hong; Rusnak, David W.; Owens, Gary; Alligood, Krystal J.; Spector, Neil L.
CS GlaxoSmithKline, Department of Discovery Medicine, Research Triangle Park, North Carolina, NC, 27709-3398, USA
SO Oncogene (2002), 21(41), 6255-6263
CODEN: ONCNES; ISSN: 0950-9232
PB Nature Publishing Group
DT Journal
LA English
AB Dual EGFR/erbB2 inhibition is an attractive therapeutic strategy for epithelial tumors, as ligand-induced erbB2/EGFR heterodimerization triggers potent proliferative and survival signals. Here we show that a small mol., GW572016, potently inhibits both EGFR and erbB2 tyrosine kinases leading to growth arrest and/or apoptosis in EGFR and erbB2-dependent tumor cell lines. GW572016 markedly reduced tyrosine phosphorylation of EGFR and erbB2, and inhibited activation of Erk1/2 and AKT, downstream effectors of proliferation and cell survival, resp. Complete inhibition of activated AKT in erbB2 overexpressing cells correlated with a 23-fold increase in apoptosis compared with vehicle controls. EGF, often elevated in cancer patients, did not reverse the inhibitory effects of GW572016. These observations were reproduced in vivo, where GW572016 treatment inhibited activation of EGFR, erbB2, Erk1/2 and AKT in human tumor xenografts. Erk1/2 and AKT represent potential biomarkers to assess the clin. activity of GW572016. Inhibition of activated AKT in EGFR or erbB2-dependent tumors by GW572016 may lead to tumor regressions when used as a monotherapy, or may enhance the anti-tumor activity of chemotherapeutics, since constitutive activation of AKT has been linked to chemo-resistance.
IT **231277-92-2**, GW 572016
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GW572016 antitumor activity: dual tyrosine kinase inhibitor blocks EGF activation of EGFR/erbB2 and downstream Erk1/2 and AKT pathways)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

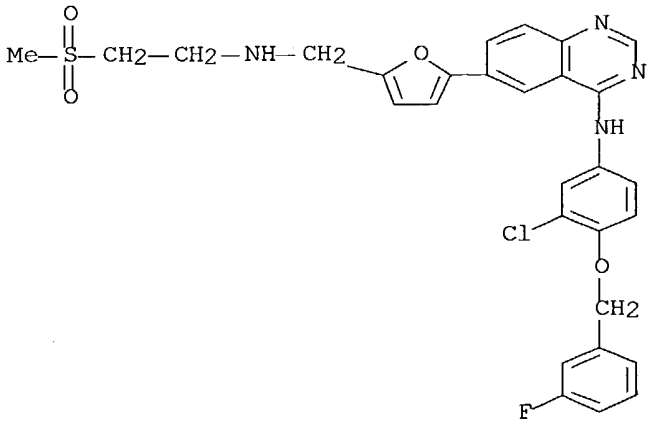


RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:555376 CAPLUS Full-text
DN 137:119644
TI 4-Quinazolineamine derivative combination with other antineoplastic agent
for cancer treatment, and compound preparation.
IN Lackey, Karen Elizabeth; Spector, Neil; Wood, Edgar Raymond, III; Xia, Wenle
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002056912	A2	20020725	WO 2002-US1130	20020114
WO 2002056912	A3	20030522		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1353693	A2	20031022	EP 2002-703127	20020114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004053946	A1	20040318	US 2003-466290	20030715
PRAI US 2001-262402P	P	20010116		
WO 2002-US1130	W	20020114		

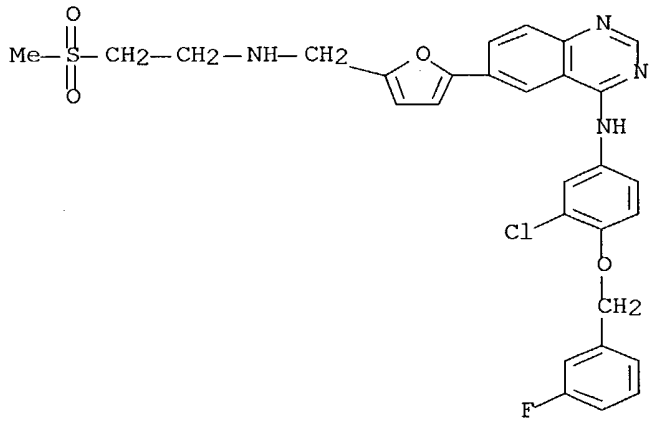
OS MARPAT 137:119644
AB A method of treating cancer is described which includes administration of a 4-quinazolineamine (preparation included) and at least one other antineoplastic agent. Also described is a pharmaceutical combination including the 4-quinazolineamines.
IT **231277-92-2P 388082-77-7P 388082-78-8P**
443883-05-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(quinazolineamine derivative combination with other antineoplastic agent
for cancer treatment, and compound preparation)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 388082-77-7 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-, bis(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

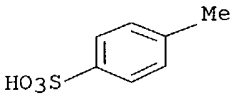
CM 1

CRN 231277-92-2
CMF C29 H26 Cl F N4 O4 S



CM 2

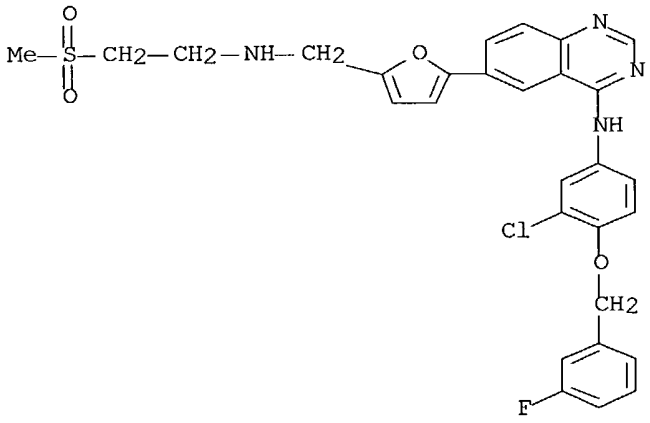
CRN 104-15-4
CMF C7 H8 O3 S



RN 388082-78-8 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-, bis(4-methylbenzenesulfonate), monohydrate (9CI) (CA INDEX NAME)

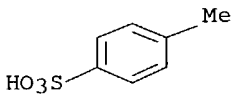
CM 1

CRN 231277-92-2
CMF C29 H26 Cl F N4 O4 S



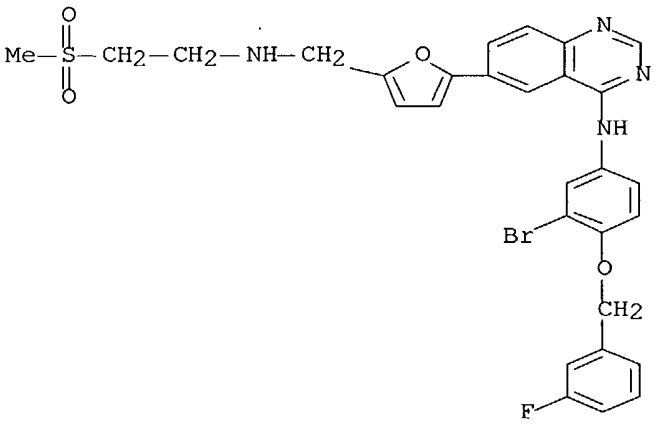
CM 2

CRN 104-15-4
CMF C7 H8 O3 S



RN 443883-05-4 CAPLUS
CN 4-Quinazolinamine, N-[3-bromo-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



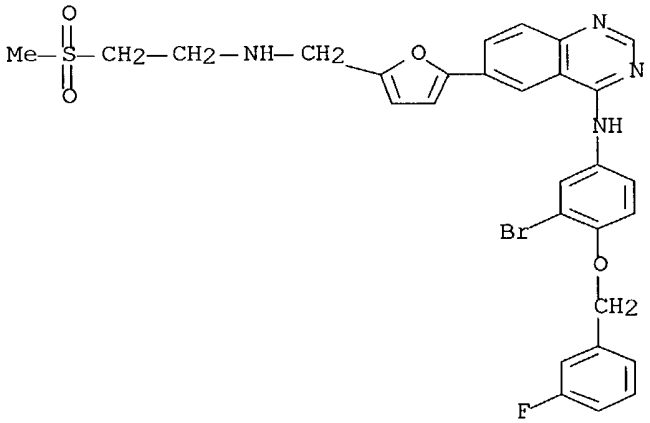
PAGE 2-A

●2 HCl

IT **388082-79-9**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinazolineamine derivative combination with other antineoplastic agent
for cancer treatment, and compound preparation)

RN 388082-79-9 CAPLUS

CN 4-Quinazolinamine, N-[3-bromo-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:31441 CAPLUS Full-text
DN 136:102396
TI Preparation of quinazoline ditosylate salts as inhibitors of erbB protein tyrosine kinases.
IN McClure, Michael Scott; Osterhout, Martin Howard; Roschangar, Frank; Sacchetti, Mark Joseph
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002002552	A1	20020110	WO 2001-US20706	20010628
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1294715	A1	20030326	EP 2001-952304	20010628
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001011947	A	20030506	BR 2001-11947	20010628
	JP 2004502687	T2	20040129	JP 2002-507804	20010628
	NO 2002006196	A	20030224	NO 2002-6196	20021223
	US 2003220354	A1	20031127	US 2003-311678	20030331
PRAI	US 2000-215508P	P	20000630		
	US 2001-271845P	P	20010227		
	WO 2001-US20706	W	20010628		

OS MARPAT 136:102396
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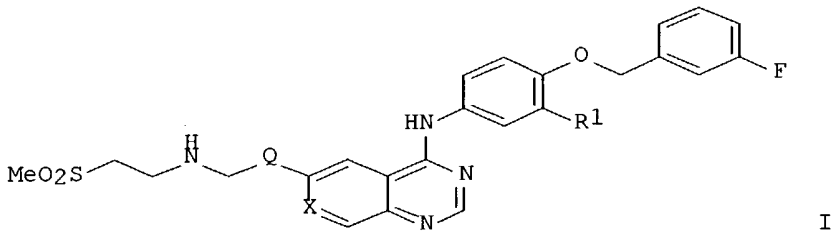

I

AB Title compds. (I; R1 = Cl, Br; X = CH, N, CF; Q = thiazolylene, furylene), were prepared Thus, 5-[4-[3-chloro-4-(3-fluorobenzyloxy)anilino]-6- quinazolinyl]furan-2-carboxaldehyde 4-methylbenzenesulfonate (preparation given), diisopropylethylamine, and 2-(methylsulfone)ethylamine were stirred 1 h in THF/IPA; he preformed imine/THF solution was transferred to a stirred suspension of NaBH(OAc)3 in THF. After 90 min, aqueous NaOH was added followed by separation of the aqueous layer treatment of the organic layer with 4-MeC6H4SO3H to

give 88% N-[3-chloro-4-[(3-fluorobenzyl)oxy]phenyl]-6-[5- [[2-(methanesulfonyl)ethyl]amino]methyl]-2-furyl-4-quinazolinamine ditosylate. This inhibited EGFr and ErbB2 at <0.10 μM.

IT **388082-80-2P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of quinazoline ditosylate salts as inhibitors of erbB protein tyrosine kinases)

RN 388082-80-2 CAPLUS

CN 4-Quinazolinamine, N-[3-bromo-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-, bis(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

CRN 388082-79-9
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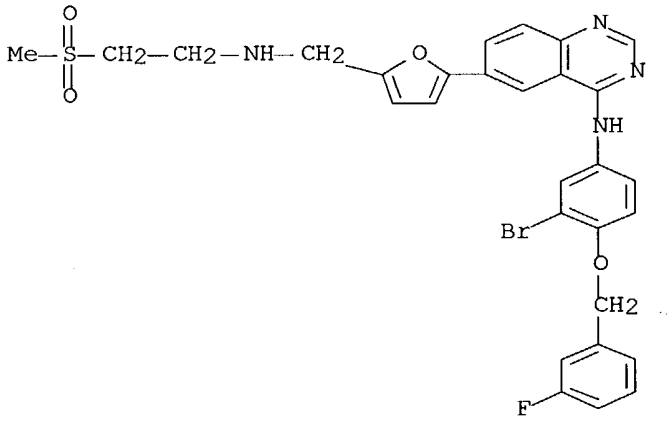
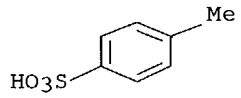


CM 2

CRN 104-15-4
CMF C7 H8 O3 S



IT **388082-77-7P**

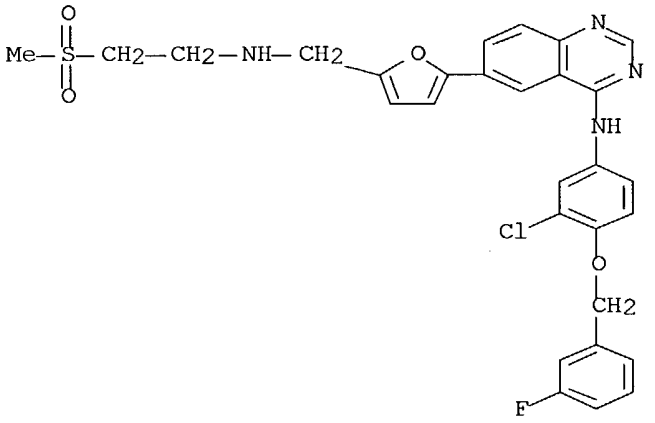
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(x-ray diffraction; preparation of quinazoline ditosylate salts as inhibitors of erbB protein tyrosine kinases)

RN 388082-77-7 CAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-, bis(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

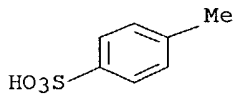
CM 1

CRN 231277-92-2
CMF C29 H26 Cl F N4 O4 S



CM 2

CRN 104-15-4
CMF C7 H8 O3 S



IT **388082-78-8P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(x-ray diffraction; preparation of quinazoline ditosylate salts as inhibitors of erbB protein tyrosine kinases)

RN 388082-78-8 CAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-, bis(4-methylbenzenesulfonate), monohydrate (9CI) (CA INDEX NAME)

CM 1

CRN 231277-92-2
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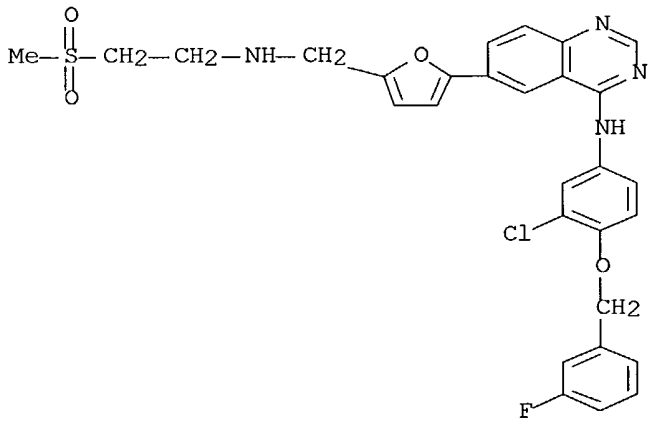

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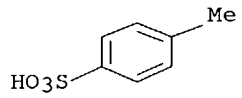
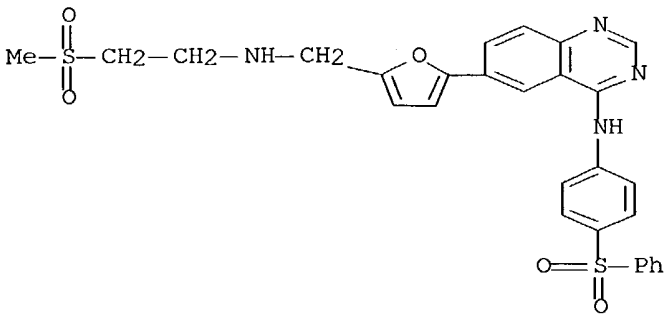
CRN 104-15-4
CMF C7 H8 O3 S



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:743253 CAPLUS Full-text
DN 136:79264
TI The characterization of novel, dual ErbB-2/EGFR, tyrosine kinase inhibitors: potential therapy for cancer
AU Rusnak, David W.; Affleck, Karen; Cockerill, Stuart G.; Stubberfield, Colin; Harris, Robert; Page, Martin; Smith, Kathryn J.; Guntrip, Stephen B.; Carter, Malcolm C.; Shaw, Robert J.; Jowett, Amanda; Stables, Jeremy; Topley, Peter; Wood, Edgar R.; Brignola, Perry S.; Kadwell, Sue H.; Reep, Bryan R.; Mullin, Robert J.; Alligood, Krystal J.; Keith, Barry R.; Crosby, Renae M.; Murray, Doris M.; Knight, W. Blaine; Gilmer, Tona M.; Lackey, Karen
CS Department of Cancer Biology, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SO Cancer Research (2001), 61(19), 7196-7203
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB The type 1 receptor tyrosine kinases constitute a family of transmembrane proteins involved in various aspects of cell growth and survival and have been implicated in the initiation and progression of several types of human malignancies. The best characterized of these proteins are the epidermal growth factor receptor (EGFR) and ErbB-2 (HER-2/neu). We have developed potent quinazoline and pyrido-[3,4-d]-pyrimidine small mols. that are dual inhibitors of ErbB-2 and EGFR. The compds. demonstrate potent in vitro inhibition of the ErbB-2 and EGFR kinase domains with IC50s <80 nM. Growth of ErbB-2- and EGFR-expressing tumor cell lines is inhibited at concns. <0.5 μM. Selectivity for tumor cell growth inhibition vs. normal human fibroblast growth inhibition ranges from 10- to >75-fold. Tumor growth in mouse s.c. xenograft models of the BT474 and HN5 cell lines is inhibited in a dose-responsive manner using oral doses of 10 and 30 mg/kg twice per day. In addition, the tested compds. caused a reduction of ErbB-2 and EGFR autophosphorylation in tumor fragments from these xenograft models. These data indicate that these compds. have potential use as therapy in the broad population of cancer patients overexpressing ErbB-2 and/or EGFR.
IT **386744-56-5**, GW 9525
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of novel, dual ErbB-2/EGFR, tyrosine kinase inhibitors and potential therapy for cancer)
RN 386744-56-5 CAPLUS
CN 4-Quinazolinamine, 6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-N-[4-(phenylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

App's

L4 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:50639 CAPLUS Full-text
DN 134:100886
TI Preparation of anilinoquinazolines as protein tyrosine kinase inhibitors
IN Cockerill, George Stuart; Lackey, Karen Elizabeth
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001004111	A1	20010118	WO 2000-US18128	20000630
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1192151	A1	20020403	EP 2000-943348	20000630
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003504363	T2	20030204	JP 2001-509721	20000630
PRAI	GB 1999-16213	A	19990709		
	GB 1999-16218	A	19990709		
	WO 2000-US18128	W	20000630		

OS MARPAT 134:100886
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

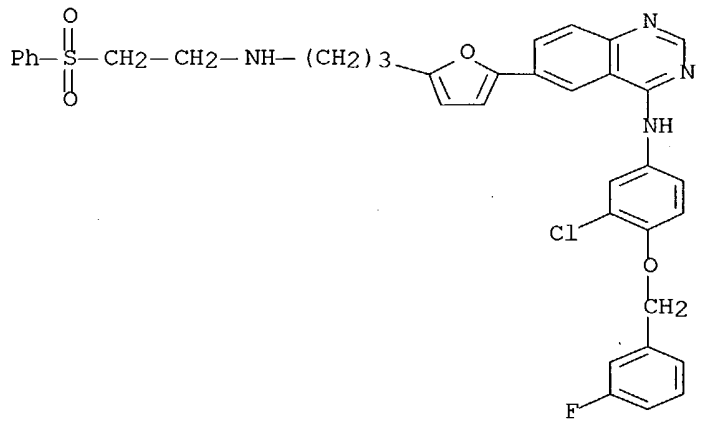
AB The title compds. [I; X = CR1 and Y = N; or X = N and Y = CR1; X = CR1 and Y = CR2; X = CR2 and Y = CR1; R1 = Ar(CH2)pZCH2CH2SO2R5 (wherein Ar = (un)substituted Ph, furan, thiophene, etc.; Z = O, S, NH, NR6; p = 1-4; R5 = alkyl substituted by 5-10 membered heterocyclic group, 3-10 membered carbocyclic group, etc.; R6 = alkyl, alkoxyalkyl, hydroxyalkyl, etc.); R2 = H, halo, OH, etc.; R3 = pyridylmethoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy; R4 = H, halo, alkyl, etc.; with the proviso that when p = 1 and Z = NH, R5 cannot represent Me] which exhibit protein tyrosine kinase inhibition, in particular erbB family kinase inhibition, and useful in treating cancer and psoriasis, were prepared E.g., a multi-step synthesis of the anilinoquinazoline II was given. Biol. data (erbB-2, erbB-4, EGFr, and cell proliferation inhibition) for the compds. I were presented.

IT **319917-32-3P 319917-33-4P 319917-34-5P**
319917-35-6P 319917-36-7P 319917-38-9P
319917-39-0P 319917-40-3P 319917-41-4P
319917-43-6P 319917-44-7P 319917-45-8P
319917-46-9P 320337-09-5P 320337-10-8P
320337-11-9P 320337-12-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)(preparation of anilinoquinazolines as protein tyrosine kinase inhibitors)

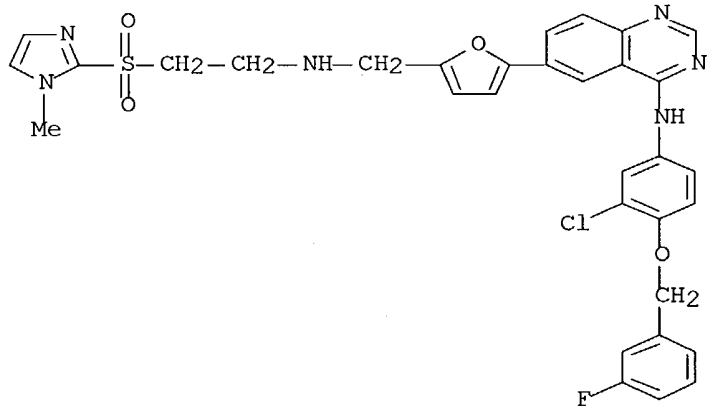
RN 319917-32-3 CAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[3-[[2-(phenylsulfonyl)ethyl]amino]propyl]-2-furanyl]- (9CI) (CA INDEX NAME)



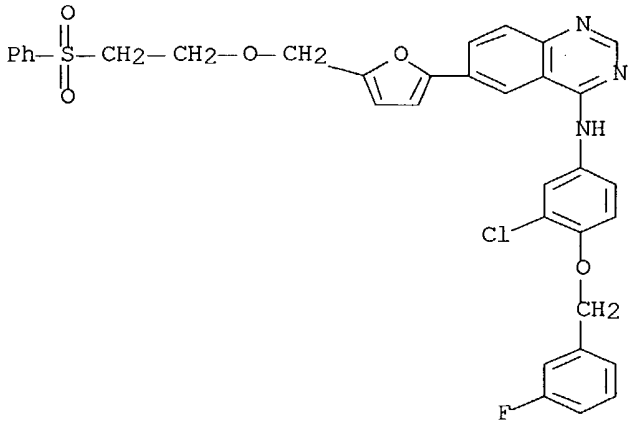
RN 319917-33-4 CAPLUS

CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-[(1-methyl-1H-imidazol-2-yl)sulfonyl]ethyl]amino]methyl]-2-furanyl]-(9CI) (CA INDEX NAME)

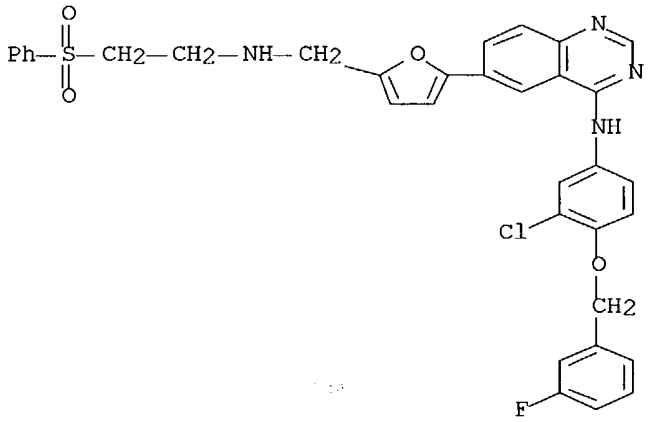


RN 319917-34-5 CAPLUS

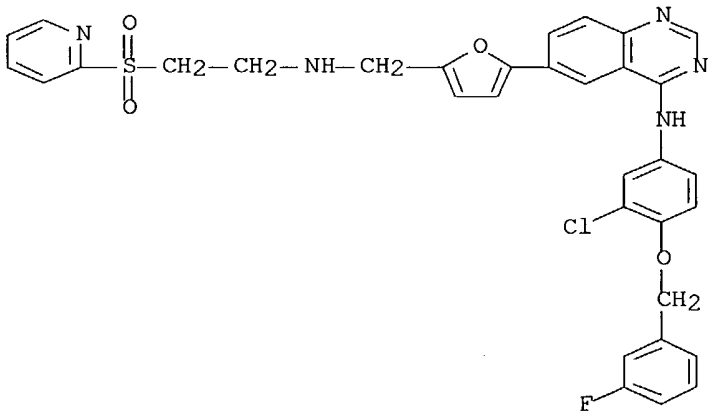
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[2-(phenylsulfonyl)ethoxy]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 319917-35-6 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(phenylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

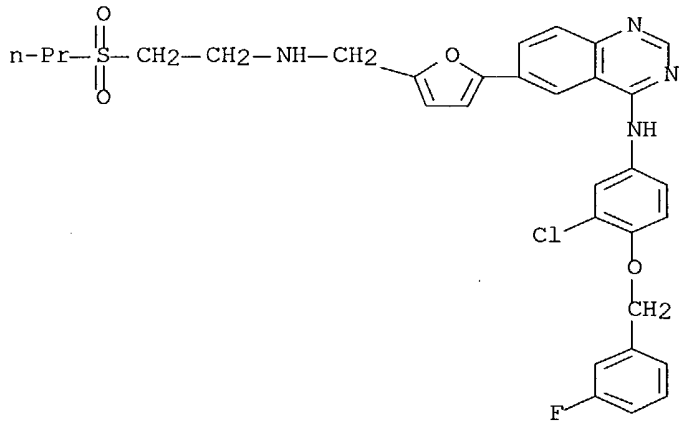


RN 319917-36-7 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(2-pyridinylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

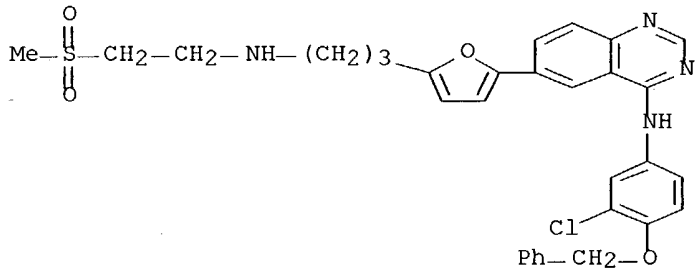


RN 319917-38-9 CAPLUS

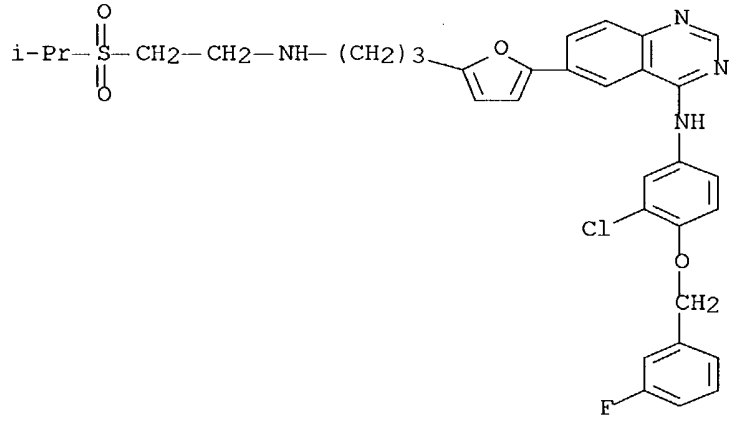
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(propylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



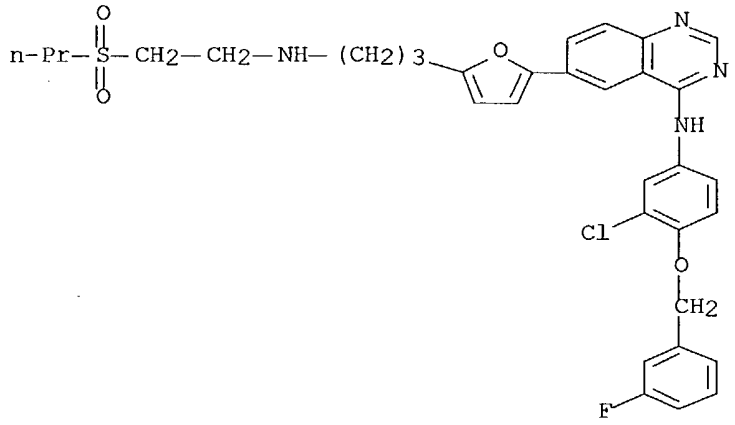
RN 319917-39-0 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-(phenylmethoxy)phenyl]-6-[5-[3-[[2-(methylsulfonyl)ethyl]amino]propyl]-2-furanyl]- (9CI) (CA INDEX NAME)



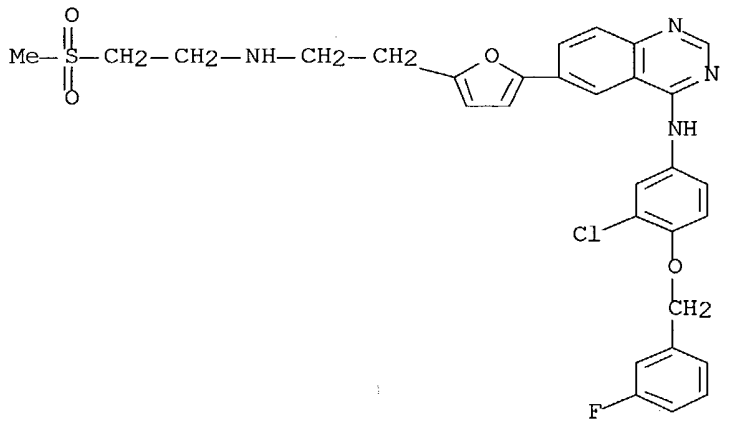
RN 319917-40-3 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[3-[[2-[(1-methylethyl)sulfonyl]ethyl]amino]propyl]-2-furanyl]- (9CI) (CA INDEX NAME)



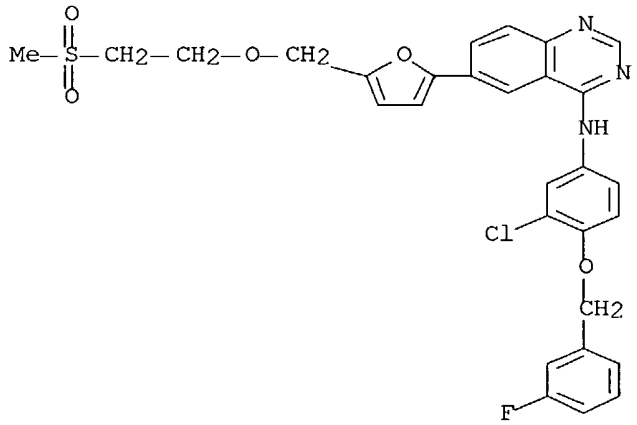
RN 319917-41-4 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[3-[[2-(propylsulfonyl)ethyl]amino]propyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 319917-43-6 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[2-[[2-(methylsulfonyl)ethyl]amino]ethyl]-2-furanyl]- (9CI) (CA INDEX NAME)

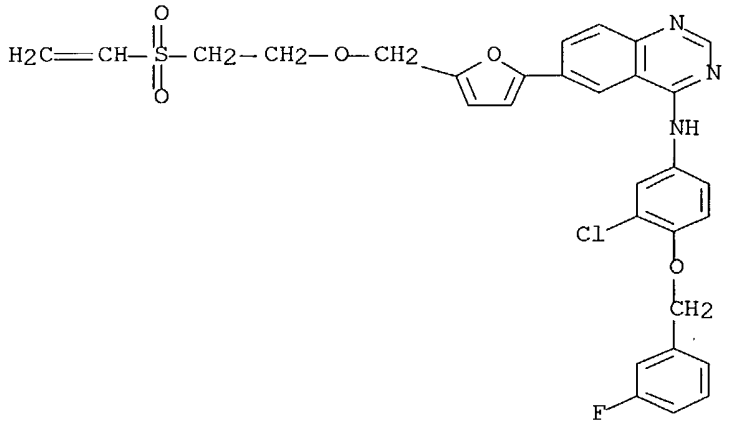


RN 319917-44-7 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[2-(methylsulfonyl)ethoxy]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)

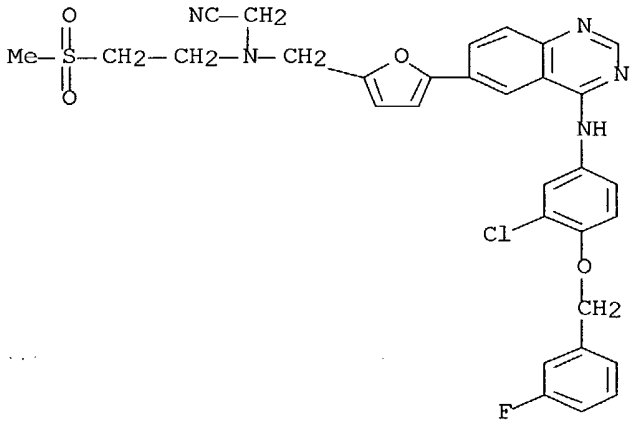


RN 319917-45-8 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-

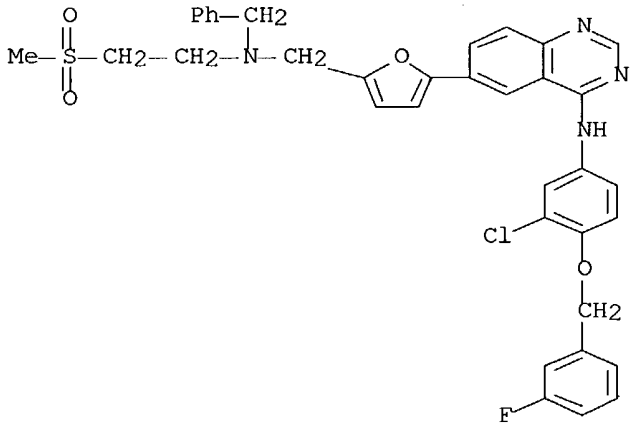
[[2-(ethenylsulfonyl)ethoxy]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



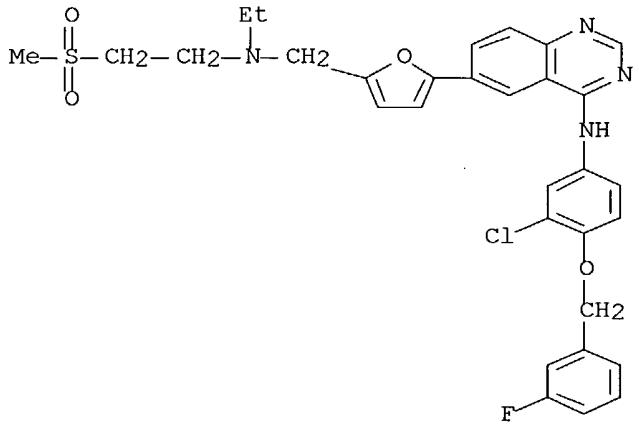
RN 319917-46-9 CAPLUS
CN Acetonitrile, [[[5-[4-[[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]amino]-6-quinazolinyl]-2-furanyl]methyl][2-(methylsulfonyl)ethyl]amino]- (9CI)(CA INDEX NAME)



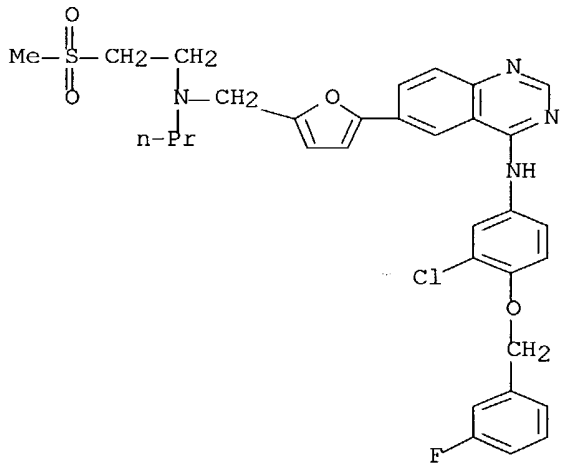
RN 320337-09-5 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl](phenylmethyl)amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



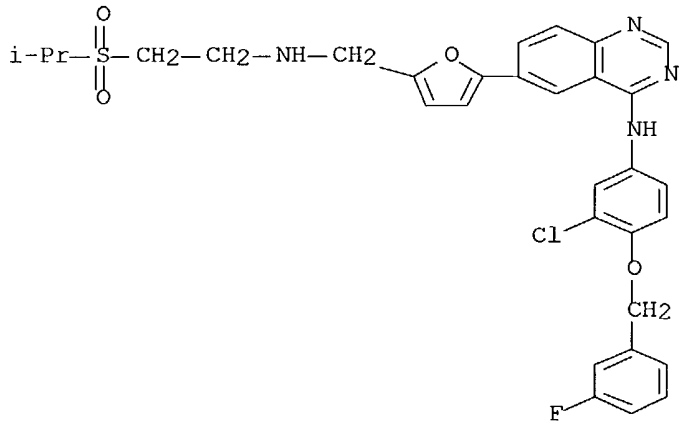
RN 320337-10-8 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[ethyl[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



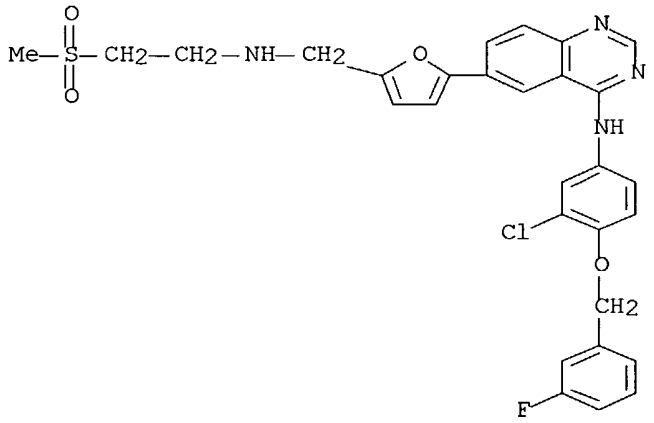
RN 320337-11-9 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]propylamino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



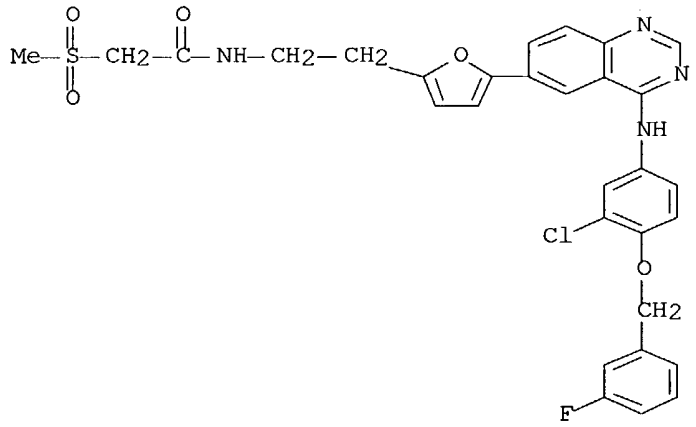
RN 320337-12-0 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-[(1-methylethyl)sulfonyl]ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



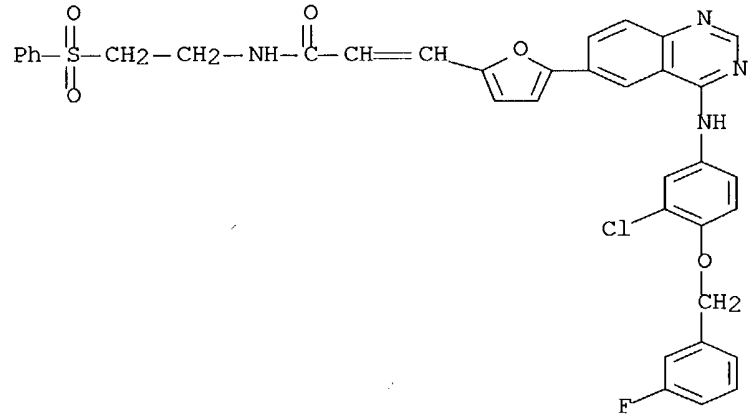
IT **231277-92-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of anilinoquinazolines as protein tyrosine kinase inhibitors)
RN 231277-92-2 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



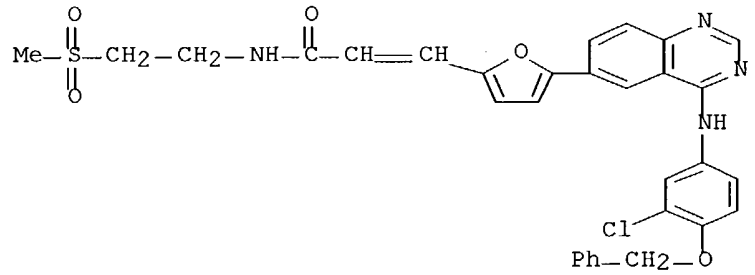
IT **320337-36-8P 320337-41-5P 320337-42-6P 320337-43-7P 320337-44-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)(preparation of anilinoquinazolines as protein tyrosine kinase inhibitors)
RN 320337-36-8 CAPLUS
CN Acetamide, N-[2-[5-[4-[[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]amino]-6-quinazolinyl]-2-furanyl]ethyl]-2-(methylsulfonyl)- (9CI) (CA INDEX NAME)



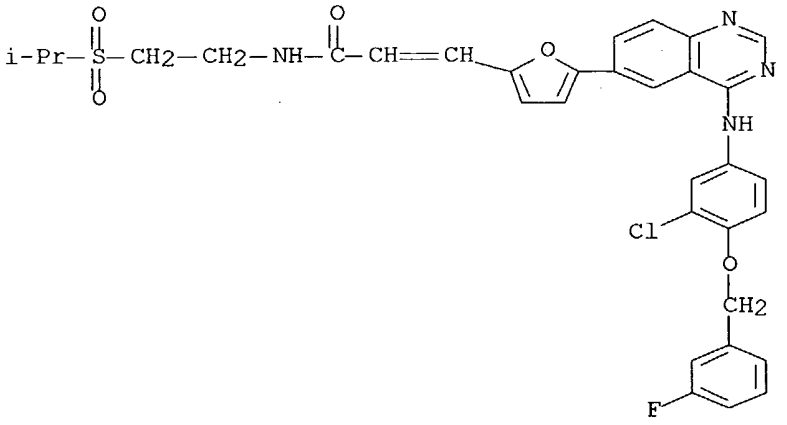
RN 320337-41-5 CAPLUS
CN 2-Propenamide, 3-[5-[4-[[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]amino]-6-quinazolinyl]-2-furanyl]-N-[2-(phenylsulfonyl)ethyl]- (9CI) (CA INDEX NAME)



RN 320337-42-6 CAPLUS
CN 2-Propenamide, 3-[5-[4-[[3-chloro-4-(phenylmethoxy)phenyl]amino]-6-quinazolinyl]-2-furanyl]-N-[2-(methylsulfonyl)ethyl]- (9CI) (CA INDEX NAME)

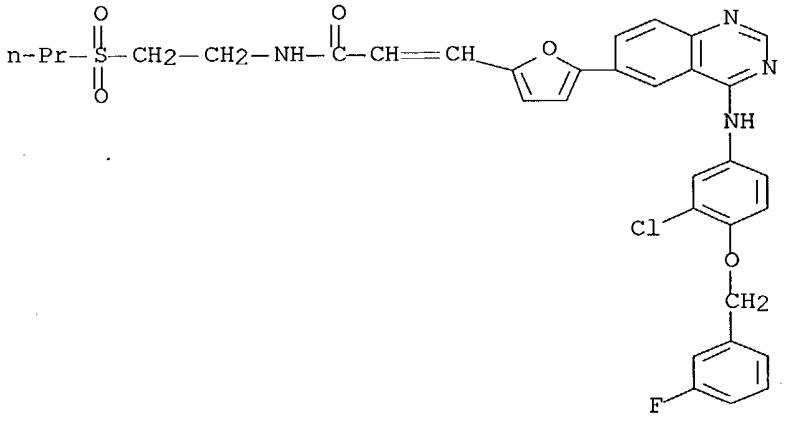


RN 320337-43-7 CAPLUS
CN 2-Propenamide, 3-[5-[4-[[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]amino]-6-quinazolinyl]-2-furanyl]-N-[2-[(1-methylethyl)sulfonyl]ethyl]- (9CI)(CA INDEX NAME)



RN 320337-44-8 CAPLUS

CN 2-Propenamide, 3-[5-[4-[[3-chloro-4-[(3-fluorophenyl)methoxy]phenyl]amino]-6-quinazolinyl]-2-furanyl]-N-[2-(propylsulfonyl)ethyl]- (9CI) (CA INDEX NAME)



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:451297 CAPLUS Full-text
DN 131:102288
TI Bicyclic heteroaromatic compounds [quinazolinamines, pyridopyrimidines, and analogs] useful as protein tyrosine kinase inhibitors
IN Carter, Malcolm Clive; Cockerill, George Stuart; Guntrip, Stephen Barry; Lackey, Karen Elizabeth; Smith, Kathryn Jane
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9935146	A1	19990715	WO 1999-EP48	19990108
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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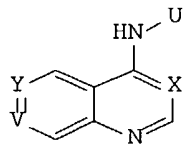

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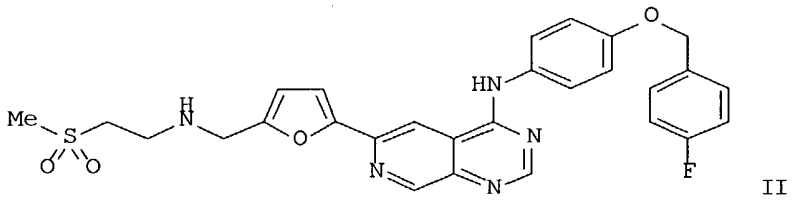


II

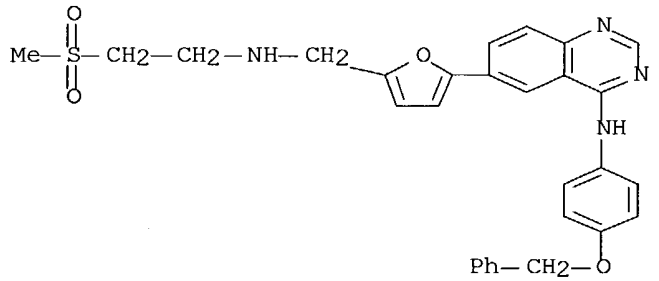
AB Title compds. I and their salts and solvates are disclosed [wherein X = N or CH; Y = CR1 and V = N; or Y = N and V = CR1; or Y = CR1 and V = CR2; or Y = CR2 and V = CR1; R1 = MeSO2CH2CH2NHCH2-Ar-, wherein Ar = (un)substituted Ph, furan, thiophene, pyrrole, or thiazole; R2 = H, halo, OH, C1-4 alkyl, C1-4 alkoxy, C1-4 alkylamino, or di[C1-4 alkyl]amino; U = Ph, pyridyl, 3H-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1H-indazolyl, 2,3-dihydro-1H-indazolyl, 1H-benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl or 1H-benzotriazolyl group, substituted by R3 and optionally by R4; R3 = (halo)benzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and (halo)benzyloxy, PhSO2, (trihalomethyl)benzyl, (trihalomethyl)benzyloxy, (R5)n-substituted phthalimido; R4 = OH, halo, C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, C1-4 alkoxy, (di)(alkyl)amino, C1-4 alkylthio, etc.; R5 = halo, C1-4 alkyl, C1-4 alkoxy; n = 0-3]. Also disclosed are methods for their preparation, pharmaceutical compns. containing them, and their use in medicine. The compds. are inhibitors of protein tyrosine kinases, and as such are useful in the treatment of cancer, psoriasis, and rheumatoid arthritis. Over 40 title compds. and numerous intermediates were prepared For example, 4,6-dichloropyrido[3,4-d]pyrimidine was condensed with 4-[(4-fluorobenzyl)oxy]aniline at the 4-chloro position, followed by Pd-catalyzed coupling with 5-(1,3-dioxolan-2-yl)-2-(tributylstannyl)furan at the 6-chloro position, hydrolysis of the dioxolane protecting group to give an aldehyde, reductive amination of the latter with MeSCH2CH2NH2, and finally S-oxidation with Oxone ® and acidification, to give title salt II.2HCl. In a methylene blue growth inhibition assay against 5 tumor cell lines, II.2HCl had an IC50 of < 5 μM against 4 of them, and an IC50 of 25-50 μM against the 5th.

IT **231277-68-2P 231278-05-0P**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(target compound, metabolism; preparation of quinazolinamines and analogs as protein tyrosine kinase inhibitors)

RN 231277-68-2 CAPLUS
CN 4-Quinazolinamine, 6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-N-[4-(phenylmethoxy)phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 231278-05-0 CAPLUS
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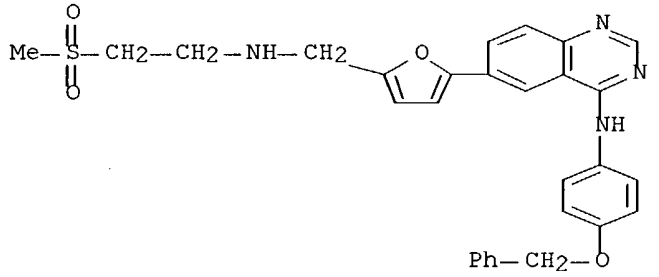

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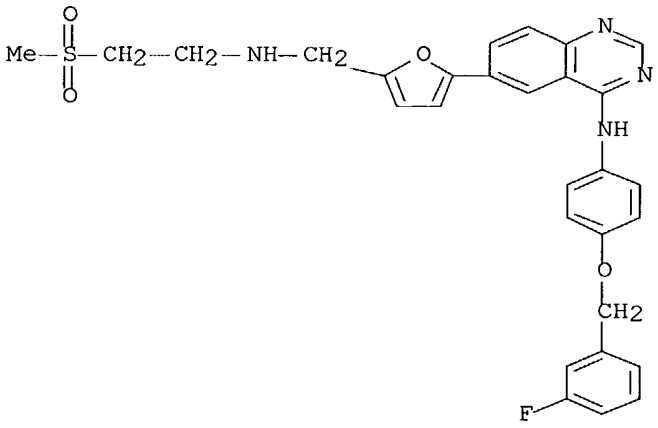
231277-74-0P 231277-80-8P 231277-81-9P
231277-82-0P 231277-83-1P 231277-85-3P
231277-90-0P 231277-91-1P 231277-92-2P
231277-96-6P 231277-97-7P 231277-99-9P
231278-00-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of quinazolinamines and analogs as protein tyrosine kinase inhibitors)

RN 231277-71-7 CAPLUS
CN 4-Quinazolinamine, N-[4-[(3-fluorophenyl)methoxy]phenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)

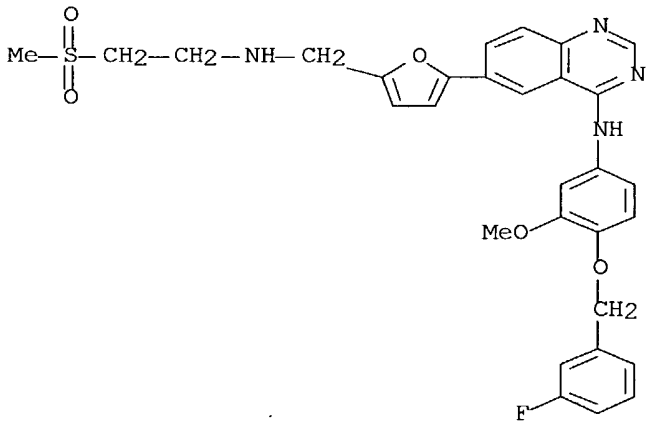
PAGE 1-A



PAGE 2-A

●2 HCl

RN 231277-72-8 CAPLUS
CN 4-Quinazolinamine, N-[4-[(3-fluorophenyl)methoxy]-3-methoxyphenyl]-6-[5-[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 231277-73-9 CAPLUS
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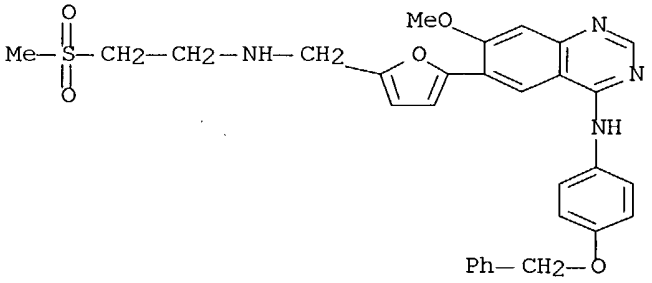
NAME)



●2 HCl

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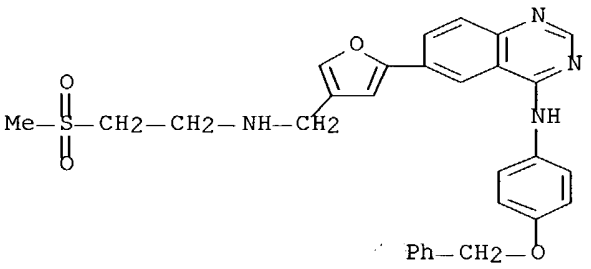

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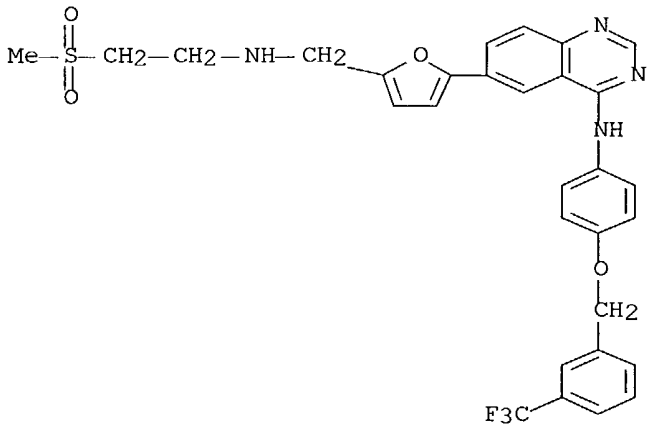

RN 231277-81-9 CAPLUS
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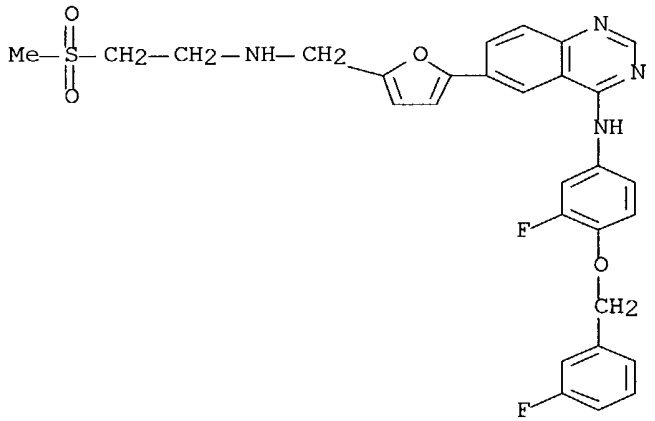

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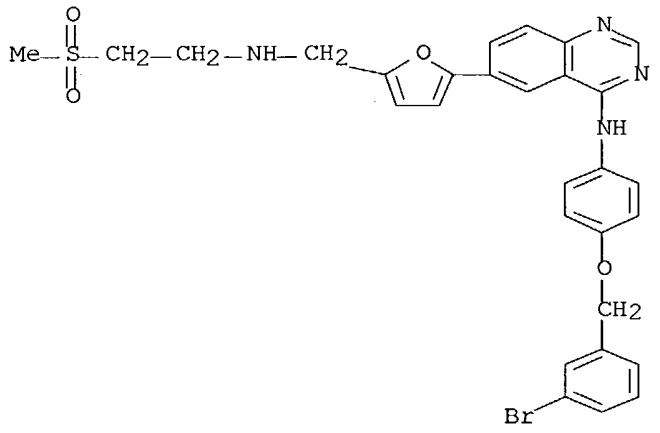

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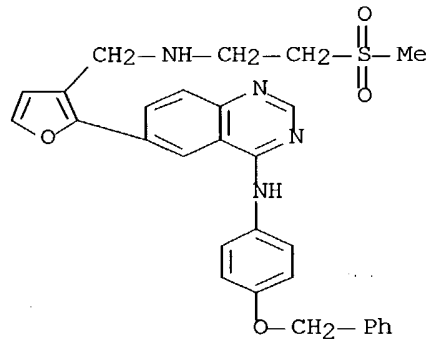

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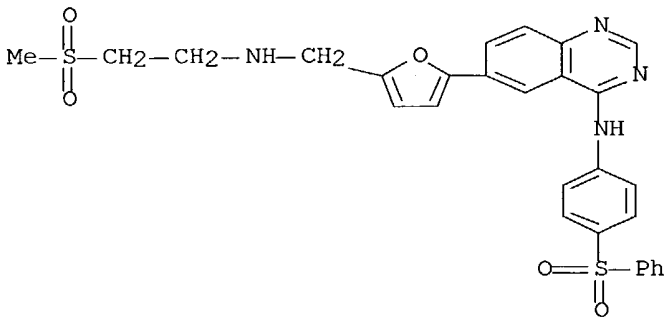

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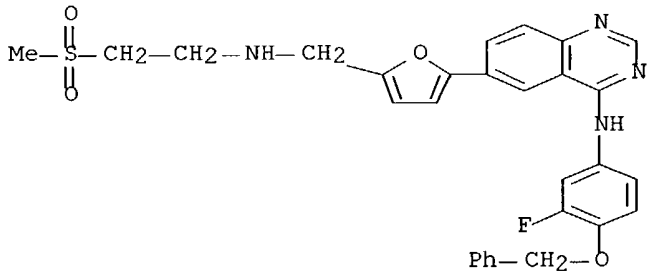

RN 231277-91-1 CAPLUS
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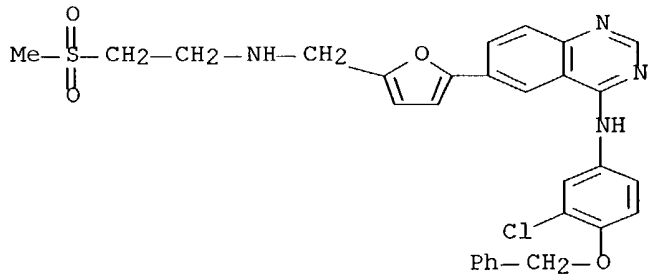

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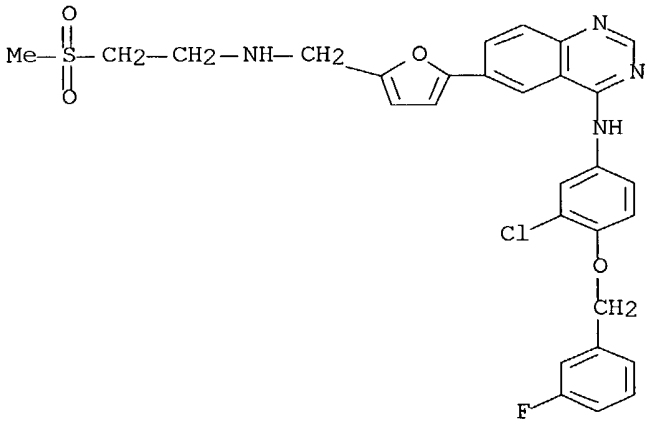

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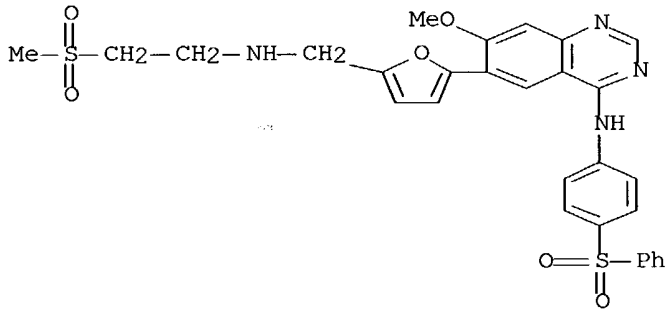

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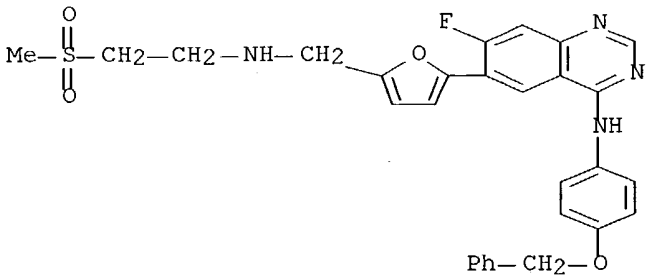

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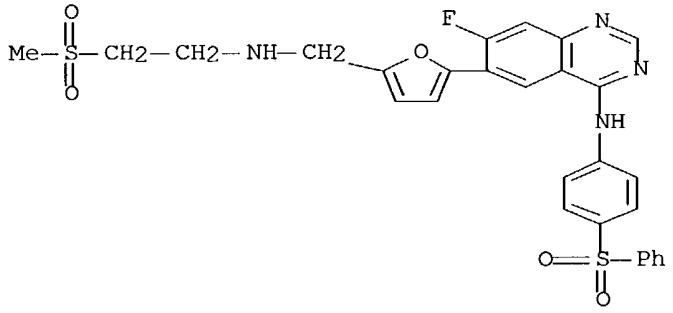

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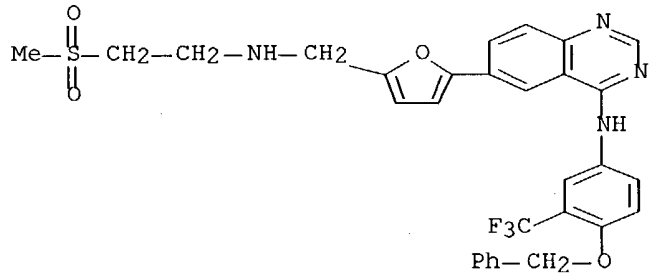

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:71133 CAPLUS Full-text
DN 128:140716
TI Preparation of azolylquinazolines and related compounds as protein tyrosine kinase inhibitors.
IN Cockerill, George Stuart; Carter, Malcolm Clive; Guntrip, Stephen Barry; Smith, Kathryn Jane
PA Glaxo Group Limited, UK; Cockerill, George Stuart; Carter, Malcolm Clive; Guntrip, Stephen Barry; Smith, Kathryn Jane
SO PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	US 6391874	B1	20020521	US 1998-214267	19981231
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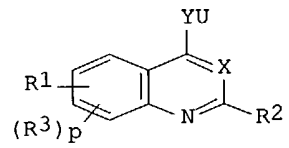


I

AB Title compds. [I; U = substituted Ph, mono- or bicyclic 5-10 membered (hetero)cyclyl; X = N, CH; Y = W(CH2), (CH2)W, W; W = O, S(O)m, NRa; Ra = H, alkyl; m = 0-2; R1 = (substituted) Ph, 5- or 6-membered heterocyclyl containing 1-4 heteroatoms selected from N, O, S(O)m; with the provision that the ring does not contain two adjacent O or S(O)m atoms and that where the ring contains only N as heteroatom(s) the ring

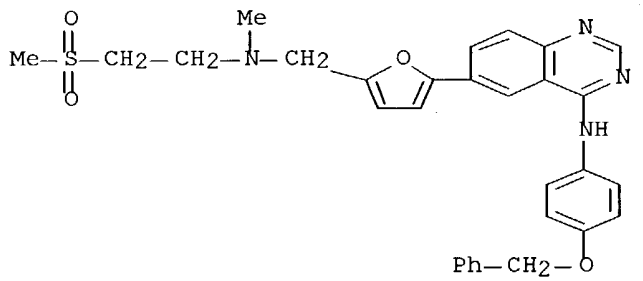
is C-linked to the quinazoline or quinoline ring; R3 = H, amino, halo, OH, NO2, CO2H, CHO, cyano, CF3, OCF3, carbamoyl, alkoxycarbonyl, Ph, PhO, pyridonyl, pyrrolidinyl, imidazolyl, dioxolanyl, arylsulfonyl, alkylsulfonyl, alkylcarbamoylalkyl, piperidinoalkoxy, thiomorpholino, etc.; 2 adjacent R3 = methylenedioxy, ethylenedioxy; p = 0-3], were prepared Thus, (S)-1-[5-[4-(1-benzyl-1H-indazol-5-ylamino)quinazolin-6-yl]furan-2- ylmethyl]pyrrolidine-2-carboxylic acid amide dihydrochloride (preparation given) inhibited BT474 human breast cancer cell proliferation with IC50 = 2 nM.

IT **202196-85-8P 202196-87-0P 202196-90-5P**
202196-91-6P 202198-10-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of azolylquinazolines and related compds. as protein tyrosine kinase inhibitors)

RN 202196-85-8 CAPLUS

CN 4-Quinazolinamine, 6-[5-[[methyl[2-(methylsulfonyl)ethyl]amino]methyl]-2-furanyl]-N-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



RN 202196-87-0 CAPLUS

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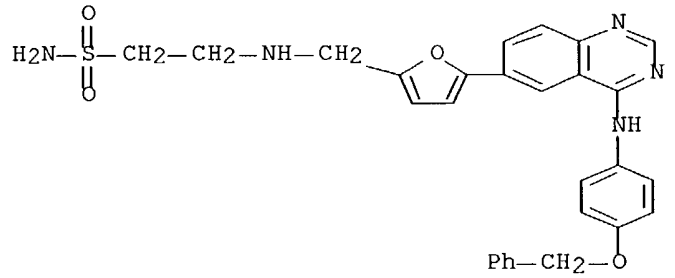

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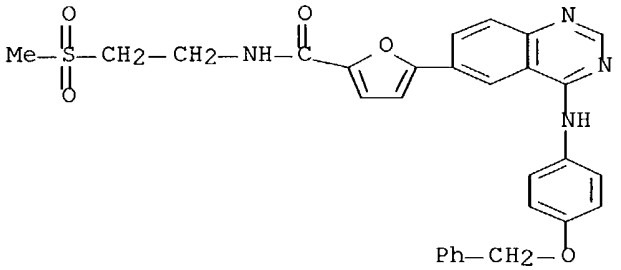
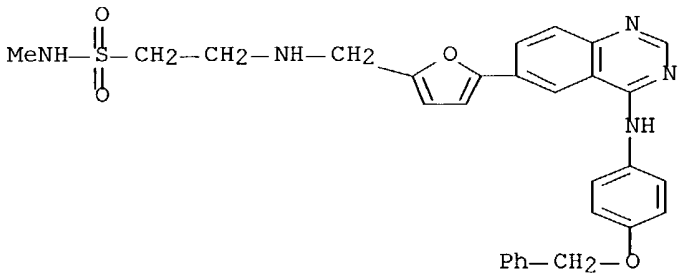
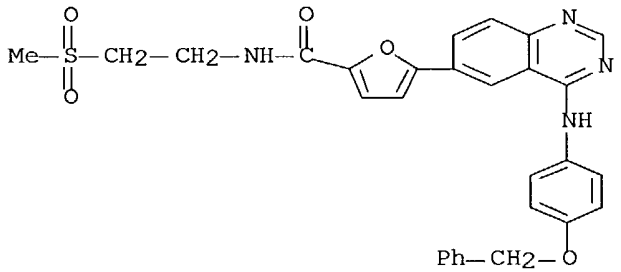


RN 202196-91-6 CAPLUS
CN Ethanesulfonamide, N-methyl-2-[[[5-[4-[[4-(phenylmethoxy)phenyl]amino]-6-quinazolinyl]-2-furanyl]methyl]amino]- (9CI) (CA INDEX NAME)



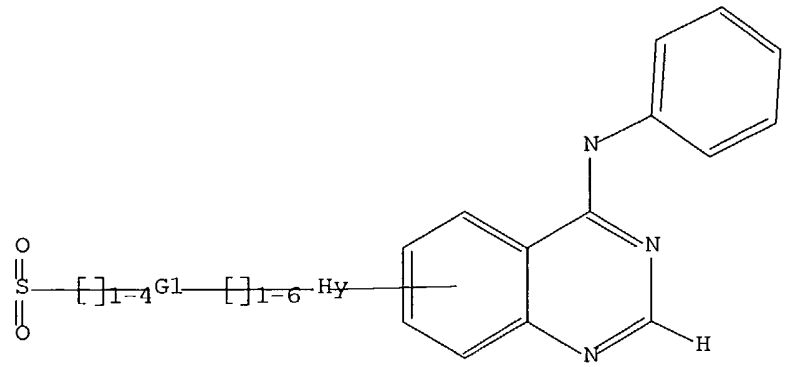
RN 202198-10-5 CAPLUS
CN 2-Furancarboxamide, N-[2-(methylsulfonyl)ethyl]-5-[4-[[4-(phenylmethoxy)phenyl]amino]-6-quinazolinyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l1; d his; log y
L1 HAS NO ANSWERS
L1 STR



G1 O,S,N

Structure attributes must be viewed using STN Express query preparation.

(FILE 'HOME' ENTERED AT 16:05:05 ON 29 JUL 2004)

FILE 'REGISTRY' ENTERED AT 16:05:18 ON 29 JUL 2004
L1 STRUCTURE UPLOADED
L2 3 S L1
L3 52 S L1 FUL

FILE 'CAPLUS' ENTERED AT 16:05:54 ON 29 JUL 2004
L4 23 S L3

FILE 'BEILSTEIN' ENTERED AT 16:06:32 ON 29 JUL 2004
L5 0 S L1
L6 0 S L1 FUL

FILE 'MARPAT' ENTERED AT 16:06:57 ON 29 JUL 2004
L7 0 S L1
L8 7 S L1 FUL
L9 0 S L8 NOT L4

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	109.42	380.52

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-16.91

STN INTERNATIONAL LOGOFF AT 16:07:33 ON 29 JUL 2004